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(54) Title: COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as colon cancer, are disclosed. Compositions may comprise one or more colon tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a colon tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as colon cancer. Diagnostic methods based on detecting a colon tumor protein, or mRNA encoding such a protein, in a sample are also provided.



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COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as colon cancer. The invention is more specifically related to polypeptides comprising at least a portion of a colon tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of colon cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although advances have been made in detection and therapy of cancer, no vaccine or other universally successful method for prevention or treatment is currently available. Current therapies, which are generally based on a combination of chemotherapy or surgery and radiation, continue to prove inadequate in many patients.

Colon cancer is the second most frequently diagnosed malignancy in the United States as well as the second most common cause of cancer death. An estimated 95,600 new cases of colon cancer will be diagnosed in 1998, with an estimated 47,700 deaths. The five-year survival rate for patients with colorectal cancer detected in an early localized stage is 92%; unfortunately, only 37% of colorectal cancer is diagnosed at this stage. The survival rate drops to 64% if the cancer is allowed to spread to adjacent organs or lymph nodes, and to 7% in patients with distant metastases.

The prognosis of colon cancer is directly related to the degree of penetration of the tumor through the bowel wall and the presence or absence of nodal involvement, consequently, early detection and treatment are especially important. Currently, diagnosis is aided by the use of screening assays for fecal occult blood, sigmoidoscopy, colonoscopy and double contrast barium enemas. Treatment

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regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. Recurrence following surgery (the most common form of therapy) is a major problem and is often the ultimate cause of death. In spite of considerable research into therapies for the disease, colon cancer remains difficult to diagnose and treat. In spite of considerable research into therapies for these and other cancers, colon cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as colon cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a colon tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ ID NO: 1-121, 123-197, 205-630, 632-684, 686, 690-691 and 694-1081; (b) variants of a sequence recited in SEQ ID NO: 1-121, 123-197, 205-630 and 632-684, 686, 690-691 and 694-1081; and (c) complements of a sequence of (a) or (b).

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a colon tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

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Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a colon tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

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Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a colon tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expresses such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be colon cancer.

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The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression
of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
(d) comparing the amount of polynucleotide detected in step (c) with the amount

detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached figures. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

SEQUENCE IDENTIFIERS

SEQ ID NO: 1 is a first determined cDNA sequence for Contig 1, showing homology to Neutrophil Gelatinase Associated Lipocalin.

SEQ ID NO: 2 is the determined cDNA sequence for Contig 2, showing no significant homology to any known genes.

SEQ ID NO: 3 is the determined cDNA sequence for Contig 4, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 4 is the determined cDNA sequence for Contig 5, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 5 is the determined cDNA sequence for Contig 9, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 6 is the determined cDNA sequence for Contig 52, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 7 is the determined cDNA sequence for Contig 6, showing boundary to Villin.

SEQ ID NO: 8 is the determined cDNA sequence for Contig 8, showing no significant homology to any known genes.

SEQ ID NO: 9 is the determined cDNA sequence for Contig 10, showing homology to Transforming Growth Factor (BIGH3).

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SEQ ID NO: 10 is the determined cDNA sequence for Contig 19, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 11 is the determined cDNA sequence for Contig 21, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 12 is the determined cDNA sequence for Contig 11, showing homology to CO-029.

SEQ ID NO: 13 is the determined cDNA sequence for Contig 55, showing homology to CO-029.

SEQ ID NO: 14 is the determined cDNA sequence for Contig 12, showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P.

SEQ ID NO: 15 is the determined cDNA sequence for Contig 13, showing no significant homology to any known gene.

SEQ ID NO: 16 is the determined cDNA sequence for Contig 14, also referred to as 14261, showing no significant homology to any known gene.

SEQ ID NO: 17 is the determined cDNA sequence for Contig 15, showing homology to Ets-Related Transcription Factor (ERT).

SEQ ID NO: 18 is the determined cDNA sequence for Contig 16, showing homology to Chromosome 5, PAC clone 228g9 (LBNL H142).

SEQ ID NO: 19 is the determined cDNA sequence for Contig 24, showing homology to Chromosome 5, PAC clone 228g9 (LBNL H142).

SEQ ID NO: 20 is the determined cDNA sequence for Contig 17, showing homology to Cytokeratin.

SEQ ID NO: 21 is the determined cDNA sequence for Contig 18, showing homology to L1-Cadherin.

SEQ ID NO: 22 is the determined cDNA sequence for Contig 20, showing no significant homology to any known gene.

SEQ ID NO: 23 is the determined cDNA sequence for Contig 22, showing homology to Bumetanide-sensitive Na-K-Cl cotransporter (NKCCl).

SEQ ID NO: 24 is the determined cDNA sequence for Contig 23, showing no significant homology to any known gene.

SEQ ID NO: 25 is the determined cDNA sequence for Contig 25, showing homology to Macrophage Inflammatory Protein 3 alpha.

SEQ ID NO: 26 is the determined cDNA sequence for Contig 26, showing homology to Laminin.

SEQ ID NO: 27 is the determined cDNA sequence for Contig 48, showing homology to Laminin.

SEQ ID NO: 28 is the determined cDNA sequence for Contig 27, showing homology to Mytobularin (MTM1).

SEQ ID NO: 29 is the determined cDNA sequence for Contig 28, showing homology to Chromosome 16 BAC clone CIT987SK-A-363E6.

SEQ ID NO: 30 is the determined cDNA sequence for Contig 29, also referred to as C751P and 14247, showing no significant homology to any known gene, but partial homology to Rat GSK-3β-interacting protein Axil homolog.

SEQ ID NO: 31 is the determined cDNA sequence for Contig 30, showing homology to Zinc Finger Transcription Factor (ZNF207).

SEQ ID NO: 32 is the determined cDNA sequence for Contig 31, showing no significant homology to any known gene, but partial homology to Mus musculus GOB-4 homolog.

SEQ ID NO: 33 is the determined cDNA sequence for Contig 35, showing no significant homology to any known gene, but partial homology to Mus musculus GOB-4 homolog.

SEQ ID NO: 34 is the determined cDNA sequence for Contig 32, showing no significant homology to any known gene.

SEQ ID NO: 35 is the determined cDNA sequence for Contig 34, showing homology to Desmoglein 2.

SEQ ID NO: 36 is the determined cDNA sequence for Contig 36, showing no significant homology to any known gene.

SEQ ID NO: 37 is the determined cDNA sequence for Contig 37, showing homology to Putative Transmembrane Protein.

SEQ ID NO: 38 is the determined cDNA sequence for Contig 38, also referred to as C796P and 14219, showing no significant homology to any known gene.

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SEQ ID NO: 39 is the determined cDNA sequence for Contig 40, showing homology to Nonspecific Cross-reacting Antigen.

SEQ ID NO: 40 is the determined cDNA sequence for Contig 41, also referred to as C799P and 14308, showing no significant homology to any known gene.

SEQ ID NO: 41 is the determined cDNA sequence for Contig 42, also referred to as C794P and 14309, showing no significant homology to any known gene.

SEQ ID NO: 42 is the determined cDNA sequence for Contig 43, showing homology to Chromosome 1 specific transcript KIAA0487.

SEQ ID NO: 43 is the determined cDNA sequence for Contig 45, showing homology to hMCM2.

SEQ ID NO: 44 is the determined cDNA sequence for Contig 46, showing homology to ETS2.

SEQ ID NO: 45 is the determined cDNA sequence for Contig 49, showing homology to Pump-1.

SEQ ID NO: 46 is the determined cDNA sequence for Contig 50, also referred to as C792P and 18323, showing no significant homology to any known gene.

SEQ ID NO: 47 is the determined cDNA sequence for Contig 51, also referred to as C795P and 14317, showing no significant homology to any known gene.

SEQ ID NO: 48 is the determined cDNA sequence for 11092, showing no significant homology to any known gene.

SEQ ID NO: 49 is the determined cDNA sequence for 11093, showing no significant homology to any known gene.

SEQ ID NO: 50 is the determined cDNA sequence for 11094, showing homology Human Putative Enterocyte Differentiation Protein.

SEQ ID NO: 51 is the determined cDNA sequence for 11095, showing homology to Human Transcriptional Corepressor hKAP1/TIF1B mRNA.

SEQ ID NO: 52 is the determined cDNA sequence for 11096, showing no significant homology to any known gene.

SEQ ID NO: 53 is the determined cDNA sequence for 11097, showing homology to Human Nonspecific Antigen.

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SEQ ID NO: 54 is the determined cDNA sequence for 11098, showing no significant homology to any known gene.

SEQ ID NO: 55 is the determined cDNA sequence for 11099, showing homology to Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEQ ID NO: 56 is the determined cDNA sequence for 11186, showing homology to Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEQ ID NO: 57 is the determined cDNA sequence for 11101, showing homology to Human Chromosome X.

SEQ ID NO: 58 is the determined cDNA sequence for 11102, showing homology to Human Chromosome X.

SEQ ID NO: 59 is the determined cDNA sequence for 11103, showing no significant homology to any known gene.

SEQ ID NO: 60 is the determined cDNA sequence for 11174, showing no significant homology to any known gene.

SEQ ID NO: 61 is the determined cDNA sequence for 11104, showing homology to Human mRNA for KIAA0154.

SEQ ID NO: 62 is the determined cDNA sequence for 11105, showing homology to Human Apurinic/Apyrimidinic Endonuclease (hap1)mRNA.

SEQ ID NO: 63 is the determined cDNA sequence for 11106, showing homology to Human Chromosome 12p13.

SEQ ID NO: 64 is the determined cDNA sequence for 11107, showing homology to Human 90 kDa Heat Shock Protein.

SEQ ID NO: 65 is the determined cDNA sequence for 11108, showing no significant homology to any known gene.

SEQ ID NO: 66 is the determined cDNA sequence for 11112, showing no significant homology to any known gene.

SEQ ID NO: 67 is the determined cDNA sequence for 11115, showing no significant homology to any known gene.

SEQ ID NO: 68 is the determined cDNA sequence for 11117, showing no significant homology to any known gene.

SEQ ID NO: 69 is the determined cDNA sequence for 11118, showing no significant homology to any known gene.

SEQ ID NO: 70 is the determined cDNA sequence for 11119, showing homology to Human Elongation Factor 1-alpha.

SEQ ID NO: 71 is the determined cDNA sequence for 11121, showing homology to Human Lamin B Receptor (LBR) mRNA.

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SEQ ID NO: 72 is the determined cDNA sequence for 11122, showing homology to H. sapiens mRNA for Novel Glucocorticoid.

SEQ ID NO: 73 is the determined cDNA sequence for 11123, showing homology to H. sapiens mRNA for snRNP protein B. 10

SEQ ID NO: 74 is the determined cDNA sequence for 11124, showing homology to Human Cisplatin Resistance Associated Beta-protein.

SEQ ID NO: 75 is the determined cDNA sequence for 11127, showing homology to M. musculus Calumenin mRNA.

SEQ ID NO: 76 is the determined cDNA sequence for 11128, showing homology to Human ras-related small GTP binding protein.

SEQ ID NO: 77 is the determined cDNA sequence for 11130, showing homology to Human Cosmid U169d2.

SEQ ID NO: 78 is the determined cDNA sequence for 11131, showing homology to H. sapiens mRNA for protein homologous to Elongation 1-g. 20

SEQ ID NO: 79 is the determined cDNA sequence for 11134, showing no significant homology to any known gene.

SEQ ID NO: 80 is the determined cDNA sequence for 11135, showing homology to H. sapiens Nieman-Pick (NPC1) mRNA.

SEQ ID NO: 81 is the determined cDNA sequence for 11137, showing homology to H. sapiens mRNA for Niecin b-chain.

SEQ ID NO: 82 is the determined cDNA sequence for 11138, showing homology to Human Endogenous Retroviral Protease mRNA.

SEQ ID NO: 83 is the determined cDNA sequence for 11139, showing homology to H. sapiens mRNA for DMBT1 protein. 30

- SEQ ID NO: 84 is the determined cDNA sequence for 11140, showing homology to H. sapiens ras GTPase activating-like protein.
- SEQ ID NO: 85 is the determined cDNA sequence for 11143, showing homology to Human Acidic Ribosomal Phosphoprotein PO mRNA.
- SEQ ID NO: 86 is the determined cDNA sequence for 11144, showing homology to H. sapiens U21 mRNA.
 - SEQ ID NO: 87 is the determined cDNA sequence for 11145, showing homology to Human GTP-binding protein.
- SEQ ID NO: 88 is the determined cDNA sequence for 11148, showing homology to H. sapiens U21 mRNA.
 - SEQ ID NO: 89 is the determined cDNA sequence for 11151, showing no significant homology to any known gene.
 - SEQ ID NO: 90 is the determined cDNA sequence for 11154, showing no significant homology to any known gene.
 - SEQ ID NO: 91 is the determined cDNA sequence for 11156, showing homology to H. sapiens Ribosomal Protein L27.
 - SEQ ID NO: 92 is the determined cDNA sequence for 11157, showing homology to H. sapiens Ribosomal Protein L27.
 - SEQ ID NO: 93 is the determined cDNA sequence for 11158, showing no significant homology to any known gene.
 - SEQ ID NO: 94 is the determined cDNA sequence for 11162, showing homology to Ag-X antigen.
 - SEQ ID NO: 95 is the determined cDNA sequence for 11164, showing homology to H. sapiens mRNA for Signal Recognition Protein sub14.
- SEQ ID NO: 96 is the determined cDNA sequence for 11165, showing homology to Human PAC 204e5/127h14.
 - SEQ ID NO: 97 is the determined cDNA sequence for 11166, showing homology to Human mRNA for KIAA0108.
- SEQ ID NO: 98 is the determined cDNA sequence for 11167, showing homology to H. sapiens mRNA for Neutrophil Gelatinase assct. Lipocalin.

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SEQ ID NO: 99 is the determined cDNA sequence for 11168, showing no significant homology to any known gene.

SEQ ID NO: 100 is the determined cDNA sequence for 11172, showing no significant homology to any known gene.

SEQ ID NO: 101 is the determined cDNA sequence for 11175, showing no significant homology to any known gene.

SEQ ID NO: 102 is the determined cDNA sequence for 11176, showing homology to Human maspin mRNA.

SEQ ID NO: 103 is the determined cDNA sequence for 11177, showing homology to Human Carcinoembryonic Antigen.

SEQ ID NO: 104 is the determined cDNA sequence for 11178, showing homology to Human A-Tubulin mRNA.

SEQ ID NO: 105 is the determined cDNA sequence for 11179, showing homology to Human mRNA for proton-ATPase-like protein.

SEQ ID NO: 106 is the determined cDNA sequence for 11180, showing homology to Human HepG2 3' region cDNA clone hmd.

SEQ ID NO: 107 is the determined cDNA sequence for 11182, showing homology to Human MHC homologous to Chicken B-Complex Protein.

SEQ ID NO: 108 is the determined cDNA sequence for 11183, showing homology to Human High Mobility Group Box (SSRP1) mRNA.

SEQ ID NO: 109 is the determined cDNA sequence for 11184, showing no significant homology to any known gene.

SEQ ID NO: 110 is the determined cDNA sequence for 11185, showing no significant homology to any known gene.

SEQ ID NO: 111 is the determined cDNA sequence for 11187, showing no significant homology to any known gene.

SEQ ID NO: 112 is the determined cDNA sequence for 11190, showing homology to Human Replication Protein A 70kDa.

SEQ ID NO: 113 is the determined cDNA sequence for Contig 47, also referred to as C797P, showing homology to Human Chromosome X clone bWXD342.

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SEQ ID NO: 114 is the determined cDNA sequence for Contig 7, showing homology to Equilibrative Nucleoside Transporter 2 (ent2).

SEQ ID NO: 115 is the determined cDNA sequence for 14235.1, also referred to as C791P, showing homology to H. sapiens chromosome 21 derived BAC containing ets-2 gene.

SEQ ID NO: 116 is the determined cDNA sequence for 14287.2, showing no significant homology to any known gene, but some degree of homology to Putative Transmembrane Protein.

SEQ ID NO: 117 is the determined cDNA sequence for 14233.1, also referred to as Contig 48, showing no significant homology to any known gene.

SEQ ID NO: 118 is the determined cDNA sequence for 14298.2, also referred to as C793P, showing no significant homology to any known gene.

SEQ ID NO: 119 is the determined cDNA sequence for 14372, also referred to as Contig 44, showing no significant homology to any known gene.

SEQ ID NO: 120 is the determined cDNA sequence for 14295, showing homology to secreted cement gland protein XAG-2 homolog.

SEQ ID NO: 121 is the determined full-length cDNA sequence for a clone showing homology to Beta IG-H3.

SEQ ID NO: 122 is the predicted amino acid sequence for the clone of SEQ ID NO: 121.

SEQ ID NO: 123 is a longer determined cDNA sequence for C751P.

SEQ ID NO: 124 is a longer determined cDNA sequence for C791P.

SEQ ID NO: 125 is a longer determined cDNA sequence for C792P.

SEQ ID NO: 126 is a longer determined cDNA sequence for C793P.

SEQ ID NO: 127 is a longer determined cDNA sequence for C794P.

SEQ ID NO: 128 is a longer determined cDNA sequence for C795P.

SEQ ID NO: 129 is a longer determined cDNA sequence for C796P.

SEQ ID NO: 130 is a longer determined cDNA sequence for C797P.

SEQ ID NO: 131 is a longer determined cDNA sequence for C798P.

SEQ ID NO: 132 is a longer determined cDNA sequence for C799P.

- SEQ ID NO: 133 is a first partial determined cDNA sequence for CoSub-3 (also known as 23569).
- SEQ ID NO: 134 is a second partial determined cDNA sequence for CoSub-3 (also known as 23569).
- SEQ ID NO: 135 is a first partial determined cDNA sequence for CoSub-13 (also known as 23579).
 - SEQ ID NO: 136 is a second partial determined cDNA sequence for CoSub-13 (also known as 23579).
- SEQ ID NO: 137 is the determined cDNA sequence for CoSub-17 (also known as 23583).
 - SEQ ID NO: 138 is the determined cDNA sequence for CoSub-19 (also known as 23585).
 - SEQ ID NO: 139 is the determined cDNA sequence for CoSub-22 (also known as 23714).
- SEQ ID NO: 140 is the determined cDNA sequence for CoSub-23 (also known as 23715).
 - SEQ ID NO: 141 is the determined cDNA sequence for CoSub-26 (also known as 23717).
- SEQ ID NO: 142 is the determined cDNA sequence for CoSub-33 (also known as 23724).
 - SEQ ID NO: 143 is the determined cDNA sequence for CoSub-34 (also known as 23725).
 - SEQ ID NO: 144 is the determined cDNA sequence for CoSub-35 (also known as 23726).
- SEQ ID NO: 145 is the determined cDNA sequence for CoSub-37 (also known as 23728).
 - SEQ ID NO: 146 is the determined cDNA sequence for CoSub-39 (also known as 23730).
- SEQ ID NO: 147 is the determined cDNA sequence for CoSub-42 (also known as 23766).

- SEQ ID NO: 148 is the determined cDNA sequence for CoSub-44 (also known as 23768).
- SEQ ID NO: 149 is the determined cDNA sequence for CoSub-47 (also known as 23771).
- 5 SEQ ID NO: 150 is the determined cDNA sequence for CoSub-54 (also known as 23778).
 - SEQ ID NO: 151 is the determined cDNA sequence for CoSub-55 (also known as 23779).
- SEQ ID NO: 152 is the determined cDNA sequence for CT1 (also known as 24099). 10
 - SEQ ID NO: 153 is the determined cDNA sequence for CT2 (also known as 24100).
 - SEQ ID NO: 154 is the determined cDNA sequence for CT3 (also known as 24101).
- 15 SEQ ID NO: 155 is the determined cDNA sequence for CT6 (also known as 24104).
 - SEQ ID NO: 156 is the determined cDNA sequence for CT7 (also known as 24105).
- SEQ ID NO: 157 is the determined cDNA sequence for CT12 (also known as 24110). 20
 - SEQ ID NO: 158 is the determined cDNA sequence for CT13 (also known as 24111).
 - SEQ ID NO: 159 is the determined cDNA sequence for CT14 (also known as 24112).
- SEQ ID NO: 160 is the determined cDNA sequence for CT15 (also known as 25 24113).
 - SEQ ID NO: 161 is the determined cDNA sequence for CT17 (also known as 24115).
- SEQ ID NO: 162 is the determined cDNA sequence for CT18 (also known as 24116). 30

- SEQ ID NO: 163 is the determined cDNA sequence for CT22 (also known as 23848).
- SEQ ID NO: 164 is the determined cDNA sequence for CT24 (also known as 23849).
- SEQ ID NO: 165 is the determined cDNA sequence for CT31 (also known as 23854).
 - SEQ ID NO: 166 is the determined cDNA sequence for CT34 (also known as 23856).
- SEQ ID NO: 167 is the determined cDNA sequence for CT37 (also known as 10 23859).
 - SEQ ID NO: 168 is the determined cDNA sequence for CT39 (also known as 23860).
 - SEQ ID NO: 169 is the determined cDNA sequence for CT40 (also known as 23861).
- SEQ ID NO: 170 is the determined cDNA sequence for CT51 (also known as 24130).
 - SEQ ID NO: 171 is the determined cDNA sequence for CT53 (also known as 24132).
- SEQ ID NO: 172 is the determined cDNA sequence for CT63 (also known as 20 24595).
 - SEQ ID NO: 173 is the determined cDNA sequence for CT88 (also known as 24608).
 - SEQ ID NO: 174 is the determined cDNA sequence for CT92 (also known as 24800).
- SEQ ID NO: 175 is the determined cDNA sequence for CT94 (also known as 24802).
 - SEQ ID NO: 176 is the determined cDNA sequence for CT102 (also known as 24805).
- SEQ ID NO: 177 is the determined cDNA sequence for CT103 (also known as 24806).

- SEQ ID NO: 178 is the determined cDNA sequence for CT111 (also known as 25520).
- SEQ ID NO: 179 is the determined cDNA sequence for CT118 (also known as 25522).
- SEQ ID NO: 180 is the determined cDNA sequence for CT121 (also known as 25523).
 - SEQ ID NO: 181 is the determined cDNA sequence for CT126 (also known as 25527).
- SEQ ID NO: 182 is the determined cDNA sequence for CT135 (also known as 25534). 10
 - SEQ ID NO: 183 is the determined cDNA sequence for CT140 (also known as 25537).
 - SEQ ID NO: 184 is the determined cDNA sequence for CT145 (also known as 25542).
- SEQ ID NO: 185 is the determined cDNA sequence for CT147 (also known as 15 25543).
 - SEQ ID NO: 186 is the determined cDNA sequence for CT148 (also known as 25544).
- SEQ ID NO: 187 is the determined cDNA sequence for CT502 (also known as 26420). 20
 - SEQ ID NO: 188 is the determined cDNA sequence for CT507 (also known as 26425).
 - SEQ ID NO: 189 is the determined cDNA sequence for CT521 (also known as 27366).
- SEO ID NO: 190 is the determined cDNA sequence for CT544 (also known as 25 27375).
 - SEQ ID NO: 191 is the determined cDNA sequence for CT577 (also known as 27385).
- SEQ ID NO: 192 is the determined cDNA sequence for CT580 (also known as 27387). 30

SEQ ID NO: 193 is the determined cDNA sequence for CT594 (also known as 27540).

SEQ ID NO: 194 is the determined cDNA sequence for CT606 (also known as 27547).

SEQ ID NO: 195 is the determined cDNA sequence for CT607 (also known as 27548).

SEQ ID NO: 196 is the determined cDNA sequence for CT599 (also known as 27903).

SEQ ID NO: 197 is the determined cDNA sequence for CT632 (also known as 10 27922).

SEQ ID NO: 198 is the predicted amino acid sequence for CT502 (SEQ ID NO: 187).

SEQ ID NO: 199 is the predicted amino acid sequence for CT507 (SEQ ID NO: 188).

SEQ ID NO: 200 is the predicted amino acid sequence for CT521 (SEQ ID NO: 189).

SEQ ID NO: 201 is the predicted amino acid sequence for CT544 (SEQ ID NO: 190).

SEQ ID NO: 202 is the predicted amino acid sequence for CT606 (SEQ ID NO: 194).

SEQ ID NO: 203 is the predicted amino acid sequence for CT607 (SEQ ID NO: 195).

SEQ ID NO: 204 is the predicted amino acid sequence for CT632 (SEQ ID NO: 197).

SEQ ID NO: 205 is the determined cDNA sequence for clone 25244.

SEQ ID NO: 206 is the determined cDNA sequence for clone 25245.

SEQ ID NO: 207 is the determined cDNA sequence for clone 25246.

SEQ ID NO: 208 is the determined cDNA sequence for clone 25248.

SEQ ID NO: 209 is the determined cDNA sequence for clone 25249.

SEQ ID NO: 210 is the determined cDNA sequence for clone 25250.

SEQ ID NO: 211 is the determined cDNA sequence for clone 25251.

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SEQ ID NO: 212 is the determined cDNA sequence for clone 25252. SEQ ID NO: 213 is the determined cDNA sequence for clone 25253. SEQ ID NO: 214 is the determined cDNA sequence for clone 25254. SEQ ID NO: 215 is the determined cDNA sequence for clone 25255. SEQ ID NO: 216 is the determined cDNA sequence for clone 25256. 5 SEQ ID NO: 217 is the determined cDNA sequence for clone 25257. SEQ ID NO: 218 is the determined cDNA sequence for clone 25259. SEQ ID NO: 219 is the determined cDNA sequence for clone 25260. SEQ ID NO: 220 is the determined cDNA sequence for clone 25261. SEQ ID NO: 221 is the determined cDNA sequence for clone 25262. 10 SEQ ID NO: 222 is the determined cDNA sequence for clone 25263. SEQ ID NO: 223 is the determined cDNA sequence for clone 25264. SEQ ID NO: 224 is the determined cDNA sequence for clone 25265. SEQ ID NO: 225 is the determined cDNA sequence for clone 25266. SEQ ID NO: 226 is the determined cDNA sequence for clone 25267. 15 SEQ ID NO: 227 is the determined cDNA sequence for clone 25268. SEQ ID NO: 228 is the determined cDNA sequence for clone 25269. SEQ ID NO: 229 is the determined cDNA sequence for clone 25271. SEQ ID NO: 230 is the determined cDNA sequence for clone 25272. SEQ ID NO: 231 is the determined cDNA sequence for clone 25273. 20 SEQ ID NO: 232 is the determined cDNA sequence for clone 25274. SEQ ID NO: 233 is the determined cDNA sequence for clone 25275. SEQ ID NO: 234 is the determined cDNA sequence for clone 25276. SEQ ID NO: 235 is the determined cDNA sequence for clone 25277. SEQ ID NO: 236 is the determined cDNA sequence for clone 25278. 25 SEQ ID NO: 237 is the determined cDNA sequence for clone 25280. SEQ ID NO: 238 is the determined cDNA sequence for clone 25281. SEQ ID NO: 239 is the determined cDNA sequence for clone 25282. SEQ ID NO: 240 is the determined cDNA sequence for clone 25283. 30 SEQ ID NO: 241 is the determined cDNA sequence for clone 25284. SEQ ID NO: 242 is the determined cDNA sequence for clone 25285.

SEQ ID NO: 243 is the determined cDNA sequence for clone 25286. SEQ ID NO: 244 is the determined cDNA sequence for clone 25287. SEQ ID NO: 245 is the determined cDNA sequence for clone 25288. SEQ ID NO: 246 is the determined cDNA sequence for clone 25289. SEQ ID NO: 247 is the determined cDNA sequence for clone 25290. 5 SEQ ID NO: 248 is the determined cDNA sequence for clone 25291. SEQ ID NO: 249 is the determined cDNA sequence for clone 25292. SEQ ID NO: 250 is the determined cDNA sequence for clone 25293. SEQ ID NO: 251 is the determined cDNA sequence for clone 25294. SEQ ID NO: 252 is the determined cDNA sequence for clone 25295. 10 SEQ ID NO: 253 is the determined cDNA sequence for clone 25296. SEQ ID NO: 254 is the determined cDNA sequence for clone 25297. SEQ ID NO: 255 is the determined cDNA sequence for clone 25418. SEQ ID NO: 256 is the determined cDNA sequence for clone 25419. SEQ ID NO: 257 is the determined cDNA sequence for clone 25420. 15 SEQ ID NO: 258 is the determined cDNA sequence for clone 25421. SEQ ID NO: 259 is the determined cDNA sequence for clone 25422. SEQ ID NO: 260 is the determined cDNA sequence for clone 25423. SEQ ID NO: 261 is the determined cDNA sequence for clone 25424. SEQ ID NO: 262 is the determined cDNA sequence for clone 25426. 20 SEQ ID NO: 263 is the determined cDNA sequence for clone 25427. SEQ ID NO: 264 is the determined cDNA sequence for clone 25428. SEQ ID NO: 265 is the determined cDNA sequence for clone 25429. SEQ ID NO: 266 is the determined cDNA sequence for clone 25430. SEQ ID NO: 267 is the determined cDNA sequence for clone 25431. 25 SEQ ID NO: 268 is the determined cDNA sequence for clone 25432. SEQ ID NO: 269 is the determined cDNA sequence for clone 25433. SEQ ID NO: 270 is the determined cDNA sequence for clone 25434. SEQ ID NO: 271 is the determined cDNA sequence for clone 25435. SEQ ID NO: 272 is the determined cDNA sequence for clone 25436. 30 SEQ ID NO: 273 is the determined cDNA sequence for clone 25437.

	SEQ ID NO: 274 is the determined cDNA sequence for clone 25438.
	SEQ ID NO: 275 is the determined cDNA sequence for clone 25439.
	SEQ ID NO: 276 is the determined cDNA sequence for clone 25440.
	SEQ ID NO: 277 is the determined cDNA sequence for clone 25441.
5	SEQ ID NO: 278 is the determined cDNA sequence for clone 25442.
	SEQ ID NO: 279 is the determined cDNA sequence for clone 25443.
	SEQ ID NO: 280 is the determined cDNA sequence for clone 25444.
	SEQ ID NO: 281 is the determined cDNA sequence for clone 25445.
	SEQ ID NO: 282 is the determined cDNA sequence for clone 25446.
10	SEQ ID NO: 283 is the determined cDNA sequence for clone 25447.
	SEQ ID NO: 284 is the determined cDNA sequence for clone 25448.
	SEQ ID NO: 285 is the determined cDNA sequence for clone 25844.
	SEQ ID NO: 286 is the determined cDNA sequence for clone 25845.
	SEQ ID NO: 287 is the determined cDNA sequence for clone 25846.
15	SEQ ID NO: 288 is the determined cDNA sequence for clone 25847.
	SEQ ID NO: 289 is the determined cDNA sequence for clone 25848.
	SEQ ID NO: 290 is the determined cDNA sequence for clone 25850.
	SEQ ID NO: 291 is the determined cDNA sequence for clone 25851.
	SEQ ID NO: 292 is the determined cDNA sequence for clone 25852.
20	SEQ ID NO: 293 is the determined cDNA sequence for clone 25853.
	SEQ ID NO: 294 is the determined cDNA sequence for clone 25854.
	SEQ ID NO: 295 is the determined cDNA sequence for clone 25855.
	SEQ ID NO: 296 is the determined cDNA sequence for clone 25856.
•	SEQ ID NO: 297 is the determined cDNA sequence for clone 25857.
25	SEQ ID NO: 298 is the determined cDNA sequence for clone 25858.
	SEQ ID NO: 299 is the determined cDNA sequence for clone 25859.
	SEQ ID NO: 300 is the determined cDNA sequence for clone 25860.
	SEQ ID NO: 301 is the determined cDNA sequence for clone 25861.
	SEQ ID NO: 302 is the determined cDNA sequence for clone 25862.
30	SEQ ID NO: 303 is the determined cDNA sequence for clone 25863.
	SEQ ID NO: 304 is the determined cDNA sequence for clone 25864.

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SEQ ID NO: 305 is the determined cDNA sequence for clone 25865. SEQ ID NO: 306 is the determined cDNA sequence for clone 25866. SEQ ID NO: 307 is the determined cDNA sequence for clone 25867. SEQ ID NO: 308 is the determined cDNA sequence for clone 25868. SEQ ID NO: 309 is the determined cDNA sequence for clone 25869. SEQ ID NO: 310 is the determined cDNA sequence for clone 25870. SEQ ID NO: 311 is the determined cDNA sequence for clone 25871. SEQ ID NO: 312 is the determined cDNA sequence for clone 25872. SEQ ID NO: 313 is the determined cDNA sequence for clone 25873. SEQ ID NO: 314 is the determined cDNA sequence for clone 25875. SEQ ID NO: 315 is the determined cDNA sequence for clone 25876. SEQ ID NO: 316 is the determined cDNA sequence for clone 25877. SEQ ID NO: 317 is the determined cDNA sequence for clone 25878. SEQ ID NO: 318 is the determined cDNA sequence for clone 25879. SEQ ID NO: 319 is the determined cDNA sequence for clone 25880. 15 SEQ ID NO: 320 is the determined cDNA sequence for clone 25881. SEQ ID NO: 321 is the determined cDNA sequence for clone 25882. SEQ ID NO: 322 is the determined cDNA sequence for clone 25883. SEQ ID NO: 323 is the determined cDNA sequence for clone 25884. SEQ ID NO: 324 is the determined cDNA sequence for clone 25885. 20 SEQ ID NO: 325 is the determined cDNA sequence for clone 25886. SEQ ID NO: 326 is the determined cDNA sequence for clone 25887. SEQ ID NO: 327 is the determined cDNA sequence for clone 25888. SEQ ID NO: 328 is the determined cDNA sequence for clone 25889. SEQ ID NO: 329 is the determined cDNA sequence for clone 25890. 25 SEQ ID NO: 330 is the determined cDNA sequence for clone 25892. SEQ ID NO: 331 is the determined cDNA sequence for clone 25894. SEQ ID NO: 332 is the determined cDNA sequence for clone 25895. SEQ ID NO: 333 is the determined cDNA sequence for clone 25896. SEQ ID NO: 334 is the determined cDNA sequence for clone 25897. 30 SEQ ID NO: 335 is the determined cDNA sequence for clone 25899.

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SEQ ID NO: 336 is the determined cDNA sequence for clone 25900. SEQ ID NO: 337 is the determined cDNA sequence for clone 25901. SEQ ID NO: 338 is the determined cDNA sequence for clone 25902. SEQ ID NO: 339 is the determined cDNA sequence for clone 25903. SEQ ID NO: 340 is the determined cDNA sequence for clone 25904. SEQ ID NO: 341 is the determined cDNA sequence for clone 25906. SEQ ID NO: 342 is the determined cDNA sequence for clone 25907. SEQ ID NO: 343 is the determined cDNA sequence for clone 25908. SEQ ID NO: 344 is the determined cDNA sequence for clone 25909. SEQ ID NO: 345 is the determined cDNA sequence for clone 25910. SEQ ID NO: 346 is the determined cDNA sequence for clone 25911. SEQ ID NO: 347 is the determined cDNA sequence for clone 25912. SEQ ID NO: 348 is the determined cDNA sequence for clone 25913. SEQ ID NO: 349 is the determined cDNA sequence for clone 25914. SEQ ID NO: 350 is the determined cDNA sequence for clone 25915. SEQ ID NO: 351 is the determined cDNA sequence for clone 25916. SEQ ID NO: 352 is the determined cDNA sequence for clone 25917. SEQ ID NO: 353 is the determined cDNA sequence for clone 25918. SEQ ID NO: 354 is the determined cDNA sequence for clone 25919. SEQ ID NO: 355 is the determined cDNA sequence for clone 25920. SEQ ID NO: 356 is the determined cDNA sequence for clone 25921. SEQ ID NO: 357 is the determined cDNA sequence for clone 25922. SEQ ID NO: 358 is the determined cDNA sequence for clone 25924. SEQ ID NO: 359 is the determined cDNA sequence for clone 25925. SEQ ID NO: 360 is the determined cDNA sequence for clone 25926. SEQ ID NO: 361 is the determined cDNA sequence for clone 25927. SEQ ID NO: 362 is the determined cDNA sequence for clone 25928. SEQ ID NO: 363 is the determined cDNA sequence for clone 25929. SEQ ID NO: 364 is the determined cDNA sequence for clone 25930. SEQ ID NO: 365 is the determined cDNA sequence for clone 25931. SEQ ID NO: 366 is the determined cDNA sequence for clone 25932.

SEQ ID NO: 367 is the determined cDNA sequence for clone 25933. SEQ ID NO: 368 is the determined cDNA sequence for clone 25934. SEQ ID NO: 369 is the determined cDNA sequence for clone 25935. SEQ ID NO: 370 is the determined cDNA sequence for clone 25936. SEQ ID NO: 371 is the determined cDNA sequence for clone 25939. 5 SEQ ID NO: 372 is the determined cDNA sequence for clone 32016. SEQ ID NO: 373 is the determined cDNA sequence for clone 32021. SEQ ID NO: 374 is the determined cDNA sequence for clone 31993. SEQ ID NO: 375 is the determined cDNA sequence for clone 31997. SEQ ID NO: 376 is the determined cDNA sequence for clone 31942. 10 SEQ ID NO: 377 is the determined cDNA sequence for clone 31937. SEQ ID NO: 378 is the determined cDNA sequence for clone 31952. SEQ ID NO: 379 is the determined cDNA sequence for clone 31992. SEQ ID NO: 380 is the determined cDNA sequence for clone 31961. SEQ ID NO: 381 is the determined cDNA sequence for clone 31964. 15 SEQ ID NO: 382 is the determined cDNA sequence for clone 32005. SEQ ID NO: 383 is the determined cDNA sequence for clone 31980. SEQ ID NO: 384 is the determined cDNA sequence for clone 31940. SEQ ID NO: 385 is the determined cDNA sequence for clone 32004. SEQ ID NO: 386 is the determined cDNA sequence for clone 31956. 20 SEQ ID NO: 387 is the determined cDNA sequence for clone 31934. SEQ ID NO: 388 is the determined cDNA sequence for clone 31998. SEQ ID NO: 389 is the determined cDNA sequence for clone 31973. SEQ ID NO: 390 is the determined cDNA sequence for clone 31976. SEQ ID NO: 391 is the determined cDNA sequence for clone 31988. 25 SEQ ID NO: 392 is the determined cDNA sequence for clone 31948. SEQ ID NO: 393 is the determined cDNA sequence for clone 32013. SEQ ID NO: 394 is the determined cDNA sequence for clone 31986. SEQ ID NO: 395 is the determined cDNA sequence for clone 31954. SEQ ID NO: 396 is the determined cDNA sequence for clone 31987. 30 SEQ ID NO: 397 is the determined cDNA sequence for clone 32029.

SEQ ID NO: 398 is the determined cDNA sequence for clone 32028. SEQ ID NO: 399 is the determined cDNA sequence for clone 32012. SEQ ID NO: 400 is the determined cDNA sequence for clone 31959. SEQ ID NO: 401 is the determined cDNA sequence for clone 32027. 5 SEQ ID NO: 402 is the determined cDNA sequence for clone 31957. SEQ ID NO: 403 is the determined cDNA sequence for clone 31950. SEQ ID NO: 404 is the determined cDNA sequence for clone 32011. SEQ ID NO: 405 is the determined cDNA sequence for clone 32022. SEQ ID NO: 406 is the determined cDNA sequence for clone 32014. 10 SEQ ID NO: 407 is the determined cDNA sequence for clone 31963. SEQ ID NO: 408 is the determined cDNA sequence for clone 31989. SEQ ID NO: 409 is the determined cDNA sequence for clone 32015. SEQ ID NO: 410 is the determined cDNA sequence for clone 32002. SEQ ID NO: 411 is the determined cDNA sequence for clone 31939. 15 SEQ ID NO: 412 is the determined cDNA sequence for clone 32003. SEQ ID NO: 413 is the determined cDNA sequence for clone 31936. SEQ ID NO: 414 is the determined cDNA sequence for clone 32007. SEQ ID NO: 415 is the determined cDNA sequence for clone 31965. SEQ ID NO: 416 is the determined cDNA sequence for clone 31935. 20 SEQ ID NO: 417 is the determined cDNA sequence for clone 32008. SEQ ID NO: 418 is the determined cDNA sequence for clone 31966. SEQ ID NO: 419 is the determined cDNA sequence for clone 32020. SEQ ID NO: 420 is the determined cDNA sequence for clone 31971. SEQ ID NO: 421 is the determined cDNA sequence for clone 31977. 25 SEQ ID NO: 422 is the determined cDNA sequence for clone 31985. SEQ ID NO: 423 is the determined cDNA sequence for clone 32023. SEQ ID NO: 424 is the determined cDNA sequence for clone 31981. SEQ ID NO: 425 is the determined cDNA sequence for clone 32006. SEQ ID NO: 426 is the determined cDNA sequence for clone 31991. SEQ ID NO: 427 is the determined cDNA sequence for clone 31995. 30 SEQ ID NO: 428 is the determined cDNA sequence for clone 32000.

SEQ ID NO: 429 is the determined cDNA sequence for clone 31990. SEQ ID NO: 430 is the determined cDNA sequence for clone 31946. SEQ ID NO: 431 is the determined cDNA sequence for clone 31938. SEQ ID NO: 432 is the determined cDNA sequence for clone 31941. SEQ ID NO: 433 is the determined cDNA sequence for clone 31982. 5 SEQ ID NO: 434 is the determined cDNA sequence for clone 31996. SEQ ID NO: 435 is the determined cDNA sequence for clone 32010. SEQ ID NO: 436 is the determined cDNA sequence for clone 31974. SEQ ID NO: 437 is the determined cDNA sequence for clone 31983. SEQ ID NO: 438 is the determined cDNA sequence for clone 31999. 10 SEQ ID NO: 439 is the determined cDNA sequence for clone 31949. SEQ ID NO: 440 is the determined cDNA sequence for clone 31947. SEQ ID NO: 441 is the determined cDNA sequence for clone 31994. SEQ ID NO: 442 is the determined cDNA sequence for clone 31958. SEQ ID NO: 443 is the determined cDNA sequence for clone 31975. 15 SEQ ID NO: 444 is the determined cDNA sequence for clone 31984. SEQ ID NO: 445 is the determined cDNA sequence for clone 32024. SEQ ID NO: 446 is the determined cDNA sequence for clone 31972. SEQ ID NO: 447 is the determined cDNA sequence for clone 31943. SEQ ID NO: 448 is the determined cDNA sequence for clone 32018. 20 SEQ ID NO: 449 is the determined cDNA sequence for clone 32026. SEQ ID NO: 450 is the determined cDNA sequence for clone 32009. SEQ ID NO: 451 is the determined cDNA sequence for clone 32019. SEQ ID NO: 452 is the determined cDNA sequence for clone 32025. SEQ ID NO: 453 is the determined cDNA sequence for clone 31967. 25 SEQ ID NO: 454 is the determined cDNA sequence for clone 31968. SEQ ID NO: 455 is the determined cDNA sequence for clone 31955. SEQ ID NO: 456 is the determined cDNA sequence for clone 31951. SEQ ID NO: 457 is the determined cDNA sequence for clone 31970. SEQ ID NO: 458 is the determined cDNA sequence for clone 31962. 30 SEQ ID NO: 459 is the determined cDNA sequence for clone 32001.

SEQ ID NO: 460 is the determined cDNA sequence for clone 31953. SEQ ID NO: 461 is the determined cDNA sequence for clone 31944. SEQ ID NO: 462 is the determined cDNA sequence for clone 31825. SEQ ID NO: 463 is the determined cDNA sequence for clone 31828. 5 SEQ ID NO: 464 is the determined cDNA sequence for clone 31830. SEQ ID NO: 465 is the determined cDNA sequence for clone 31841. SEQ ID NO: 466 is the determined cDNA sequence for clone 31847. SEQ ID NO: 467 is the determined cDNA sequence for clone 31850. SEQ ID NO: 468 is the determined cDNA sequence for clone 31852. 10 SEQ ID NO: 469 is the determined cDNA sequence for clone 31855. SEQ ID NO: 470 is the determined cDNA sequence for clone 31858. SEQ ID NO: 471 is the determined cDNA sequence for clone 31861. SEQ ID NO: 472 is the determined cDNA sequence for clone 31868. SEQ ID NO: 473 is the determined cDNA sequence for clone 31870. SEQ ID NO: 474 is the determined cDNA sequence for clone 31872. 15 SEQ ID NO: 475 is the determined cDNA sequence for clone 31873. SEQ ID NO: 476 is the determined cDNA sequence for clone 31877. SEQ ID NO: 477 is the determined cDNA sequence for clone 31878. SEQ ID NO: 478 is the determined cDNA sequence for clone 31885. SEQ ID NO: 479 is the determined cDNA sequence for clone 31888. 20 SEQ ID NO: 480 is the determined cDNA sequence for clone 31890. SEQ ID NO: 481 is the determined cDNA sequence for clone 31893. SEQ ID NO: 482 is the determined cDNA sequence for clone 31898. SEQ ID NO: 483 is the determined cDNA sequence for clone 31901. SEQ ID NO: 484 is the determined cDNA sequence for clone 31909. 25 SEQ ID NO: 485 is the determined cDNA sequence for clone 31910. SEQ ID NO: 486 is the determined cDNA sequence for clone 31914. SEQ ID NO: 487 is the determined cDNA sequence for contig 1. SEQ ID NO: 488 is the determined cDNA sequence for contig 2. SEQ ID NO: 489 is the determined cDNA sequence for contig 3. 30 SEQ ID NO: 490 is the determined cDNA sequence for contig 4.

SEQ ID NO: 491 is the determined cDNA sequence for contig 5. SEQ ID NO: 492 is the determined cDNA sequence for contig 6. SEQ ID NO: 493 is the determined cDNA sequence for contig 7. SEQ ID NO: 494 is the determined cDNA sequence for contig 8. SEQ ID NO: 495 is the determined cDNA sequence for contig 9. 5 SEQ ID NO: 496 is the determined cDNA sequence for contig 10. SEQ ID NO: 497 is the determined cDNA sequence for contig 11 SEQ ID NO: 498 is the determined cDNA sequence for contig 12 SEQ ID NO: 499 is the determined cDNA sequence for contig 13. SEQ ID NO: 500 is the determined cDNA sequence for contig 14. 10 SEQ ID NO: 501 is the determined cDNA sequence for contig 15. SEQ ID NO: 502 is the determined cDNA sequence for contig 16. SEQ ID NO: 503 is the determined cDNA sequence for contig 17. SEQ ID NO: 504 is the determined cDNA sequence for contig 18. SEQ ID NO: 505 is the determined cDNA sequence for contig 19. 15 SEQ ID NO: 506 is the determined cDNA sequence for contig 20. SEQ ID NO: 507 is the determined cDNA sequence for contig 21. SEQ ID NO: 508 is the determined cDNA sequence for contig 22. SEQ ID NO: 509 is the determined cDNA sequence for contig 23. SEQ ID NO: 510 is the determined cDNA sequence for contig 24. 20 SEQ ID NO: 511 is the determined cDNA sequence for contig 25. SEQ ID NO: 512 is the determined cDNA sequence for contig 26. SEQ ID NO: 513 is the determined cDNA sequence for contig 27. SEQ ID NO: 514 is the determined cDNA sequence for contig 28. SEQ ID NO: 515 is the determined cDNA sequence for contig 29. 25 SEQ ID NO: 516 is the determined cDNA sequence for contig 30. SEQ ID NO: 517 is the determined cDNA sequence for contig 31. SEQ ID NO: 518 is the determined cDNA sequence for contig 32. SEQ ID NO: 519 is the determined cDNA sequence for contig 33. SEQ ID NO: 520 is the determined cDNA sequence for contig 34. 30 SEQ ID NO: 521 is the determined cDNA sequence for contig 35.

SEQ ID NO: 522 is the determined cDNA sequence for contig 36. SEQ ID NO: 523 is the determined cDNA sequence for contig 37. SEQ ID NO: 524 is the determined cDNA sequence for contig 38. SEQ ID NO: 525 is the determined cDNA sequence for contig 39. 5 SEQ ID NO: 526 is the determined cDNA sequence for contig 40. SEQ ID NO: 527 is the determined cDNA sequence for contig 41. SEQ ID NO: 528 is the determined cDNA sequence for contig 42. SEQ ID NO: 529 is the determined cDNA sequence for contig 43. SEQ ID NO: 530 is the determined cDNA sequence for contig 44. SEQ ID NO: 531 is the determined cDNA sequence for contig 45. 10 SEQ ID NO: 532 is the determined cDNA sequence for contig 46. SEQ ID NO: 533 is the determined cDNA sequence for contig 47. SEQ ID NO: 534 is the determined cDNA sequence for contig 48. SEQ ID NO: 535 is the determined cDNA sequence for contig 49. 15 SEQ ID NO: 536 is the determined cDNA sequence for contig 50. SEQ ID NO: 537 is the determined cDNA sequence for contig 51. SEQ ID NO: 538 is the determined cDNA sequence for contig 52. SEQ ID NO: 539 is the determined cDNA sequence for contig 53. SEQ ID NO: 540 is the determined cDNA sequence for contig 54. 20 SEQ ID NO: 541 is the determined cDNA sequence for contig 55. SEQ ID NO: 542 is the determined cDNA sequence for contig 56. SEQ ID NO: 543 is the determined cDNA sequence for contig 58. SEQ ID NO: 544 is the determined cDNA sequence for contig 59. SEQ ID NO: 545 is the determined cDNA sequence for contig 60. 25 SEQ ID NO: 546 is the determined cDNA sequence for contig 61. SEQ ID NO: 547 is the determined cDNA sequence for contig 62. SEQ ID NO: 548 is the determined cDNA sequence for contig 63. SEQ ID NO: 549 is the determined cDNA sequence for contig 64. SEQ ID NO: 550 is the determined cDNA sequence for contig 65. SEQ ID NO: 551 is the determined cDNA sequence for contig 66. 30 SEQ ID NO: 552 is the determined cDNA sequence for contig 67.

	SEQ ID NO: 553 is the determined cDNA sequence for contig 68.
-	SEQ ID NO: 554 is the determined cDNA sequence for contig 69.
	SEQ ID NO: 555 is the determined cDNA sequence for contig 70.
	SEQ ID NO: 556 is the determined cDNA sequence for contig 71.
5	SEQ ID NO: 557 is the determined cDNA sequence for contig 72.
	SEQ ID NO: 558 is the determined cDNA sequence for contig 73.
	SEQ ID NO: 559 is the determined cDNA sequence for contig 74.
	SEQ ID NO: 560 is the determined cDNA sequence for contig 75.
	SEQ ID NO: 561 is the determined cDNA sequence for contig 76.
10	SEQ ID NO: 562 is the determined cDNA sequence for contig 77.
	SEQ ID NO: 563 is the determined cDNA sequence for contig 78.
	SEQ ID NO: 564 is the determined cDNA sequence for contig 79.
	SEQ ID NO: 565 is the determined cDNA sequence for contig 80.
	SEQ ID NO: 566 is the determined cDNA sequence for contig 81.
15 .	SEQ ID NO: 567 is the determined cDNA sequence for contig 82.
	SEQ ID NO: 568 is the determined cDNA sequence for contig 83.
	SEQ ID NO: 569 is the determined cDNA sequence for clone CS1-101.
	SEQ ID NO: 570 is the determined cDNA sequence for clone CS1-102.
	SEQ ID NO: 571 is the determined cDNA sequence for clone CS1-104.
20	SEQ ID NO: 572 is the determined cDNA sequence for clone CS1-105.
	SEQ ID NO: 573 is the determined 3' cDNA sequence for clone CS1-106.
	SEQ ID NO: 574 is the determined 5' cDNA sequence for clone CS1-106
	SEQ ID NO: 575 is the determined cDNA sequence for clone CS1-114.
	SEQ ID NO: 576 is the determined cDNA sequence for clone CS1-118.
25	SEQ ID NO: 577 is the determined cDNA sequence for clone CS1-120.
	SEQ ID NO: 578 is the determined cDNA sequence for clone CS1-123.
	SEQ ID NO: 579 is the determined 3' cDNA sequence for clone CS1-124
	SEQ ID NO: 580 is the determined 5' cDNA sequence for clone CS1-124
	SEQ ID NO: 581 is the determined cDNA sequence for clone CS1-128.
30	SEQ ID NO: 582 is the determined cDNA sequence for clone CS1-132.
	SEQ ID NO: 583 is the determined cDNA sequence for clone CS1-136.

SEQ ID NO: 584 is the determined cDNA sequence for clone CS1-137. SEQ ID NO: 585 is the determined cDNA sequence for clone CS1-139. SEQ ID NO: 586 is the determined cDNA sequence for clone CS1-141. SEQ ID NO: 587 is the determined cDNA sequence for clone CS1-152. 5 SEQ ID NO: 588 is the determined cDNA sequence for clone CS1-154. SEQ ID NO: 589 is the determined cDNA sequence for clone CS1-156. SEQ ID NO: 590 is the determined cDNA sequence for clone CS1-158. SEQ ID NO: 591 is the determined cDNA sequence for clone CS1-160. SEQ ID NO: 592 is the determined cDNA sequence for clone CS1-168. 10 SEQ ID NO: 593 is the determined cDNA sequence for clone CS1-169. SEQ ID NO: 594 is the determined cDNA sequence for clone CS1-171. SEQ ID NO: 595 is the determined cDNA sequence for clone CS1-176. SEQ ID NO: 596 is the determined cDNA sequence for clone CS1-178. SEQ ID NO: 597 is the determined cDNA sequence for clone CS1-180. SEQ ID NO: 598 is the determined cDNA sequence for clone CS1-183. 15 SEQ ID NO: 599 is the determined cDNA sequence for clone CS1-184. SEQ ID NO: 600 is the determined cDNA sequence for clone CS1-187. SEQ ID NO: 601 is the determined cDNA sequence for clone CS1-190. SEQ ID NO: 602 is the determined cDNA sequence for clone CS1-194. SEQ ID NO: 603 is the determined cDNA sequence for clone CS1-195. 20 SEQ ID NO: 604 is the determined cDNA sequence for clone CS1-196. SEQ ID NO: 605 is the determined cDNA sequence for clone CS1-197. SEQ ID NO: 606 is the determined cDNA sequence for clone CS1-200. SEQ ID NO: 607 is the determined cDNA sequence for clone CS1-206. 25 . SEQ ID NO: 608 is the determined cDNA sequence for clone CS1-207. SEQ ID NO: 609 is the determined cDNA sequence for clone CS1-234. SEQ ID NO: 610 is the determined cDNA sequence for clone CS1-238. SEQ ID NO: 611 is the determined cDNA sequence for clone CS1-239. SEQ ID NO: 612 is the determined cDNA sequence for clone CS1-243. SEQ ID NO: 613 is the determined cDNA sequence for clone CS1-246. 30 SEQ ID NO: 614 is the determined cDNA sequence for clone CS1-249.

SEQ ID NO: 615 is the determined cDNA sequence for clone CS1-250. SEQ ID NO: 616 is the determined cDNA sequence for clone CS1-252. SEQ ID NO: 617 is the determined cDNA sequence for clone CT502. SEQ ID NO: 618 is the determined cDNA sequence for clone CT507. SEQ ID NO: 619 is the determined cDNA sequence for clone CT521. 5 SEQ ID NO: 620 is the determined cDNA sequence for clone CT544. SEQ ID NO: 621 is the determined cDNA sequence for clone CT577. SEQ ID NO: 622 is the determined cDNA sequence for clone CT580. SEQ ID NO: 623 is the determined cDNA sequence for clone CT594. SEQ ID NO: 624 is the determined cDNA sequence for clone CT606. 10 SEQ ID NO: 625 is the determined cDNA sequence for clone CT607. SEQ ID NO: 626 is the determined cDNA sequence for clone CT599. SEQ ID NO: 627 is the determined cDNA sequence for clone CT632. SEQ ID NO: 628 is the determined cDNA sequence for clone 35691. SEQ ID NO: 629 is the determined cDNA sequence for clone 35707. 15 SEQ ID NO: 630 is the determined cDNA sequence for clone CSE-2. SEQ ID NO: 631 is the amino acid sequence for clone CSE-2. SEQ ID NO: 632 is the determined cDNA sequence for clone CT2-1. SEQ ID NO: 633 is the determined cDNA sequence for clone CT2-6. SEQ ID NO: 634 is the determined cDNA sequence for clone CT2-8. 20 SEQ ID NO: 635 is the determined cDNA sequence for clone CT2-9. SEQ ID NO: 636 is the determined cDNA sequence for clone CT2-12. SEQ ID NO: 637 is the determined cDNA sequence for clone CT2-15. SEQ ID NO: 638 is the determined cDNA sequence for clone CT2-16. SEQ ID NO: 639 is the determined cDNA sequence for clone CT2-17. 25 SEQ ID NO: 640 is the determined cDNA sequence for clone CT2-19. SEQ ID NO: 641 is the determined cDNA sequence for clone CT2-23. SEQ ID NO: 642 is the determined cDNA sequence for clone CT2-25. SEQ ID NO: 643 is the determined cDNA sequence for clone CT2-27. SEQ ID NO: 644 is the determined cDNA sequence for clone CT2-35. 30 SEQ ID NO: 645 is the determined cDNA sequence for clone CT2-39.

SEO ID NO: 646 is the determined cDNA sequence for clone CT2-41. SEO ID NO: 647 is the determined cDNA sequence for clone CT2-43. SEQ ID NO: 648 is the determined cDNA sequence for clone CT2-44. SEQ ID NO: 649 is the determined cDNA sequence for clone CT2-53. SEQ ID NO: 650 is the determined cDNA sequence for clone CT2-54. 5 SEO ID NO: 651 is the determined cDNA sequence for clone CT2-55. SEO ID NO: 652 is the determined cDNA sequence for clone CT2-57. SEQ ID NO: 653 is the determined cDNA sequence for clone CT2-60. SEQ ID NO: 654 is the determined cDNA sequence for clone CT2-64. SEQ ID NO: 655 is the determined cDNA sequence for clone CT2-67. 10 SEQ ID NO: 656 is the determined cDNA sequence for clone CT2-68. SEO ID NO: 657 is the determined cDNA sequence for clone CT2-75. SEQ ID NO: 658 is the determined cDNA sequence for clone CT2-79. SEQ ID NO: 659 is the determined cDNA sequence for clone CT2-109. SEQ ID NO: 660 is the determined cDNA sequence for clone CT2-112. 15 SEQ ID NO: 661 is the determined cDNA sequence for clone CT2-127. SEQ ID NO: 662 is the determined cDNA sequence for clone CT2-129. SEO ID NO: 663 is the determined cDNA sequence for clone CT2-156. SEQ ID NO: 664 is the determined cDNA sequence for clone CT2-162. SEQ ID NO: 665 is the determined cDNA sequence for clone CT2-167. 20 SEQ ID NO: 666 is the determined cDNA sequence for clone CT2-169. SEO ID NO: 667 is the determined cDNA sequence for clone CT2-172. SEQ ID NO: 668 is the determined cDNA sequence for clone CT2-173. SEO ID NO: 669 is the determined cDNA sequence for clone CT2-174. SEO ID NO: 670 is the determined cDNA sequence for clone CT2-177. 25 SEQ ID NO: 671 is the determined cDNA sequence for clone CT2-181. SEO ID NO: 672 is the determined cDNA sequence for clone CT2-191. SEQ ID NO: 673 is the determined cDNA sequence for clone CT2-192. SEQ ID NO: 674 is the determined cDNA sequence for clone CT2-207. SEO ID NO: 675 is the determined cDNA sequence for clone CT2-222. 30 SEQ ID NO: 676 is the determined cDNA sequence for clone CT2-223.

15

SEQ ID NO: 677 is the determined cDNA sequence for clone CT2-233.

SEQ ID NO: 678 is the determined cDNA sequence for clone CT2-244.

SEQ ID NO: 679 is the determined cDNA sequence for clone CT2-257.

SEQ ID NO: 680 is the determined cDNA sequence for clone CT2-279.

SEQ ID NO: 681 is the determined cDNA sequence for clone CT2-288.

SEQ ID NO: 682 is the determined cDNA sequence for clone CT2-291.

SEQ ID NO:683 is the full-length cDNA sequence for human PAC (SEQ ID NOs: 18 and 19).

SEQ ID NO:684 is the full-length cDNA sequence for murine homologue of human PAC (SEQ ID NO: 683).

SEQ ID NO:685 is the predicted amino acid sequence for the clone of SEQ ID NO:683.

SEQ ID NO:686 is a longer determined cDNA sequence for clone CoSub-19 (SEQ ID NO:138).

SEQ ID NO:687 is the predicted amino acid sequence for the clone of SEQ ID NO:686.

SEQ ID NO:688 is the nucleotide sequence of the M13 forward primer.

SEQ ID NO:689 is the nucleotide sequence of the M13 reverse primer.

SEQ ID NO:690 is a longer determined cDNA sequence for C799P (SEQ ID NO:40), showing homology to homo sapiens NADH/NADPH thyroid oxidase p138-tox mRNA.

SEQ ID NO:691 is a longer determined cDNA sequence for C794P (SEQ ID NO:41).

SEQ ID NO:692 is the predicted amino acid sequence for the clone of SEQ ID NO:690.

SEQ ID NO:693 is the predicted amino acid sequence for the clone of SEQ ID NO:691.

SEQ ID NO: 694 is the determined cDNA sequence for clone R0093:A03.

SEQ ID NO: 695 is the determined cDNA sequence for clone R0093:A10.

		SEQ	ID	NO:	696	is	the	determined	cDNA	sequence	tor	cione
	R0093:A11.	SEO	ID	NO.	697	is	the	determined	cDNA	sequence	for	clone
	R0093:A12.	DDQ	110	110.	0,7	10	•			4		
5		SEQ	ID	NO:	698	is	the	determined	cDNA	sequence	for	clone
	R0093:B03.	er.o	ID	NO.	600	i.	tha	determined	cDNA	cegnence	for	clone
	R0093:B04.	SEQ	ענ	NO:	099	12	ine	determined	CDIVA	sequence	101	Clone
		SEQ	ID	NO:	700	is	the	determined	cDNA	sequence	for	clone
10	R0093:B09.	aro.	TT)	NO.	701	:-	41	datamainad	oDNI A	gagyanaa	for	olone.
	R0093:B10.	SEQ	ענ	NO:	701	15	ine	determined	CDNA	sequence	101	Cione
		SEQ	ID	NO:	702	is	the	determined	cDNA	sequence	for	clone
	R0093:B11.	CEO.	ID	NO.	702	:~	th a	determined	οDNI Λ	ceavence	for	clone
15	R0093:B12.	SEQ	עו	NO:	/03	15	ille	determined	CDINA	sequence	101	Clone
		SEQ	ID	NO:	704	is	the	determined	cDNA	sequence	for	clone
	R0093:C01.	SEO	m	NO.	705	ic	the	determined	cDNA	seguence	for	clone
20	R0093:C03.	SEQ	ענ	NO.	703	12	ше	determined	CDIVA	sequence	101	Clone
		SEQ	ID	NO:	706	is	the	determined	cDNA	sequence	for	clone
	R0093:C04.	SEO.	TD	NO.	707	io	the	determined	cDNA	seguence	for	cione
	R0093:C06.	SEQ	ענ	NO.	707	13	ше	determmed	CDNA	sequence	101	CIONO
25		SEQ	ID	NO:	708	is	the	determined	cDNA	sequence	for	clone
	R0093:C08.	, SEO	m	NO.	700	ia	tha	determined	aDNIA	cequence	for	clone
	R0093:C09.	SEQ	ענ	MO;	709	18	ше	acterminea	ODNA	sequence	101	CIONE
		SEQ	ID	NO:	710	is	the	determined	cDNA	sequence	for	clone
30	R0093:C10.	or.	m	NIO	711		11.	Antonia - 3	°DYI Y	0000000	f a	- مام
		SEO	ıυ	NU:	/11	18	tne	determined	CUNA	sequence	TOL	cione

R0093:C11. SEQ ID NO: 712 is the determined cDNA sequence for clone R0093:C12. SEQ ID NO: 713 is the determined cDNA sequence for clone R0093:D01. SEQ ID NO: 714 is the determined cDNA sequence for clone R0093:D02. SEQ ID NO: 715 is the determined cDNA sequence for clone R0093:D03. SEQ ID NO: 716 is the determined cDNA sequence for clone 10 R0093:D04. SEQ ID NO: 717 is the determined cDNA sequence for clone R0093:D05. SEQ ID NO: 718 is the determined cDNA sequence for clone R0093:D06. 15 SEQ ID NO: 719 is the determined cDNA sequence for clone R0093:D07. SEQ ID NO: 720 is the determined cDNA sequence for clone R0093:D08. SEQ ID NO: 721 is the determined cDNA sequence for clone 20 R0093:D10. SEQ ID NO: 722 is the determined cDNA sequence for clone R0093:D11. SEQ ID NO: 723 is the determined cDNA sequence for clone R0093:E02. 25 SEQ ID NO: 724 is the determined cDNA sequence for clone R0093:E03. SEQ ID NO: 725 is the determined cDNA sequence for clone R0093:E04. SEQ ID NO: 726 is the determined cDNA sequence for clone 30 R0093:E06.

	D0000 700	SEQ	ID	NO:	727	is	the	determined	cDNA	sequence	for	clone
	R0093:E07.	SEQ	ID	NO:	728	is	the	determined	cDNA	sequence	for	clone
	R0093:E08.									Î		
5	R0093:E09.	SEQ	ID	NO:	729	is	the	determined	cDNA	sequence	for	clone
	K0093.E09.	SEQ	ID	NO:	730	is	the	determined	cDNA	sequence	for	clone
	R0093:E10.											
10	R0093:E11.	SEQ	ID	NO:	731	is	the	determined	cDNA	sequence	for	clone
10		SEQ	ID	NO:	732	is	the	determined	cDNA	sequence	for	clone
	R0093:F02.	077.0		370	700	•			70.7.1		6	
	R0093:F03.	SEQ	ID	NO:	733	18	the	determined	cDNA	sequence	for	clone
15		SEQ	ID	NO:	734	is	the	determined	cDNA	sequence	for	clone
	R0093:F04.	SEO	מז	NO.	735	ie	the	determined	cDNA	seguence	for	clone
	R0093:F05.	DLQ	ענו	110.	755	15	inc	determined	CDIVI	sequence	101	CIOILC
		SEQ	ID	NO:	736	is	the	determined	cDNA	sequence	for	clone
20	R0093:F06.	SEQ	ID	NO:	737	is	the	determined	cDNA	sequence	for	clone
	R0093:F08.									•		
	R0093:F09.	SEQ	ID	NO:	738	is	the	determined	cDNA	sequence	for	clone
25	K0093.F09.	SEQ	ID	NO:	739	is	the	determined	cDNA	sequence	for	clone
	R0093:F10.											
•	R0093:F12.	SEQ	ID	NO:	740	is	the	determined	cDNA	sequence	for	clone
	10055.1 12.	SEQ	ID	NO:	741	is	the	determined	cDNA	sequence	for	clone
30	R0093:G01.											
		SEQ	ID	NO:	742	is	the	determined	cDNA	sequence	for	clone

R0093:G03. SEQ ID NO: 743 is the determined cDNA sequence for clone R0093:G04. SEQ ID NO: 744 is the determined cDNA sequence for clone R0093:G06. SEQ ID NO: 745 is the determined cDNA sequence for clone R0093:G07. SEQ ID NO: 746 is the determined cDNA sequence for clone R0093:G08. SEQ ID NO: 747 is the determined cDNA sequence for clone 10 R0093:G09. SEQ ID NO: 748 is the determined cDNA sequence for clone R0093:G10. SEQ ID NO: 749 is the determined cDNA sequence for clone R0093:G11. 15 SEQ ID NO: 750 is the determined cDNA sequence for clone R0093:G12. SEQ ID NO: 751 is the determined cDNA sequence for clone R0093:H02. SEQ ID NO: 752 is the determined cDNA sequence for clone 20 R0093:H03. SEQ ID NO: 753 is the determined cDNA sequence for clone R0093:H04. SEQ ID NO: 754 is the determined cDNA sequence for clone R0093:H05. 25 SEQ ID NO: 755 is the determined cDNA sequence for clone R0093:H07. SEQ ID NO: 756 is the determined cDNA sequence for clone R0093:H08. SEQ ID NO: 757 is the determined cDNA sequence for clone 30 R0093:H09.

SEQ ID NO: 758 is the determined cDNA sequence for clone R0093:H10. SEQ ID NO: 759 is the determined cDNA sequence for clone R0093:H11. SEQ ID NO: 760 is the determined cDNA sequence for clone 5 R0094:A03. SEQ ID NO: 761 is the determined cDNA sequence for clone R0094:A05. SEQ ID NO: 762 is the determined cDNA sequence for clone R0094:A06. 10 SEQ ID NO: 763 is the determined cDNA sequence for clone R0094:A07. SEQ ID NO: 764 is the determined cDNA sequence for clone R0094:A09. SEO ID NO: 765 is the determined cDNA sequence for clone 15 R0094:A10. SEQ ID NO: 766 is the determined cDNA sequence for clone R0094:A12. SEQ ID NO: 767 is the determined cDNA sequence for clone R0094:B03. 20 SEO ID NO: 768 is the determined cDNA sequence for clone R0094:B06. SEQ ID NO: 769 is the determined cDNA sequence for clone R0094:B08. SEQ ID NO: 770 is the determined cDNA sequence for clone 25 R0094:B11. SEO ID NO: 771 is the determined cDNA sequence for clone R0094:B12. SEQ ID NO: 772 is the determined cDNA sequence for clone R0094:C01. 30 SEQ ID NO: 773 is the determined cDNA sequence for clone

R0094:C02. SEQ ID NO: 774 is the determined cDNA sequence for clone R0094:C03. SEQ ID NO: 775 is the determined cDNA sequence for clone R0094:C05. SEQ ID NO: 776 is the determined cDNA sequence for clone R0094:C06. SEQ ID NO: 777 is the determined cDNA sequence for clone R0094:C08. SEQ ID NO: 778 is the determined cDNA sequence for clone 10 R0094:C09. SEQ ID NO: 779 is the determined cDNA sequence for clone R0094:C10. SEQ ID NO: 780 is the determined cDNA sequence for clone R0094:C11. SEQ ID NO: 781 is the determined cDNA sequence for clone R0094:C12. SEQ ID NO: 782 is the determined cDNA sequence for clone R0094:D01. SEQ ID NO: 783 is the determined cDNA sequence for clone 20 R0094:D02. SEQ ID NO: 784 is the determined cDNA sequence for clone R0094:D03. SEQ ID NO: 785 is the determined cDNA sequence for clone R0094:D04. 25 SEQ ID NO: 786 is the determined cDNA sequence for clone R0094:D05. SEQ ID NO: 787 is the determined cDNA sequence for clone R0094:D07. SEQ ID NO: 788 is the determined cDNA sequence for clone 30 R0094:D08.

		SEQ	ID	NO:	789	is	the	determined	cDNA	sequence	for	clone
	R0094:D09.								73.7.		,	
	R0094:D10.	SEQ	ID	NO:	790	is	the	determined	cDNA	sequence	ior	clone
5	10071.210.	SEQ	ID	NO:	791	is	the	determined	cDNÁ	sequence	for	clone
	R0094:D12.											
	R0094:E01.	SEQ	ID	NO:	792	is	the	determined	cDNA	sequence	for	clone
	K0094.E01.	SEQ	ID	NO:	793	is	the	determined	cDNA	sequence	for	clone
10	R0094:E02.											
	D0004 F02	SEQ	ID	NO:	794	is	the	determined	cDNA	sequence	for	clone
	R0094:E03.	SEQ	ID	NO:	795	is	the	determined	cDNA	sequence	for	clone
	R0094:E05.									-		
15		SEQ	ID	NO:	796	is	the	determined	cDNA.	sequence	for	clone
	R0094:E06.	SEO	ID	NO:	797	is	the	determined	cDNA	sequence	for	clone
	R0094:E07.	224		2.0.	,,,					1		
		SEQ	ID	NO:	798	is	the	determined	cDNA	sequence	for	clone
20	R0094:E08.	SFO	ΙD	NO:	799	ie	the	determined	cDNA	sequence	for	clone
	R0094:E09.	DLQ	110	110.	133	13	uic	determined	ODIVII	sequence	101	Olone
		SEQ	ID	NO:	800	is	the	determined	cDNA	sequence	for	clone
	R0094:E10.	SEO.	ID	NO.	001	i.	tha	dataminad	aDNI A	coguence	for	alone
25	R0094:E11.	SEQ	ענ	NO:	901	15	me	determined	CDNA	sequence	101	
		SEQ	ID	NO:	802	is	the	determined	cDNA	sequence	for	clone
	R0094:E12.	~~~							***		6	•
30	R0094:F01.	SEQ	ID	NO:	803	18	the	determined	cDNA	sequence	tor	clone
		SEO	ID.	NO∙	804	is	the	determined	cDNA	sequence	for	clone

R0094:F03. SEQ ID NO: 805 is the determined cDNA sequence for clone R0094:F05. SEQ ID NO: 806 is the determined cDNA sequence for clone R0094:F06. SEQ ID NO: 807 is the determined cDNA sequence for clone R0094:F07. SEQ ID NO: 808 is the determined cDNA sequence for clone R0094:F08. SEQ ID NO: 809 is the determined cDNA sequence for clone 10 R0094:F09. SEQ ID NO: 810 is the determined cDNA sequence for clone R0094:F10. SEQ ID NO: 811 is the determined cDNA sequence for clone R0094:F11. 15 SEQ ID NO: 812 is the determined cDNA sequence for clone R0094:F12. SEQ ID NO: 813 is the determined cDNA sequence for clone R0094:G02. SEQ ID NO: 814 is the determined cDNA sequence for clone 20 R0094:G03. SEQ ID NO: 815 is the determined cDNA sequence for clone R0094:G04. SEQ ID NO: 816 is the determined cDNA sequence for clone R0094:G06. 25 SEQ ID NO: 817 is the determined cDNA sequence for clone R0094:G07. SEQ ID NO: 818 is the determined cDNA sequence for clone R0094:G08. SEQ ID NO: 819 is the determined cDNA sequence for clone 30 R0094:G10.

		SEQ	ID	NO:	820	is	the	determined	cDNA	sequence	for	clone
	R0094:G11.	SEO	מז	NO:	821	ic	the	determined	cDNA	sequence	for	clone
	R0094:G12.	SEQ	ענג	110.	021	13	ше	determined	ODIVI	soqueneo	101	010110
5	K0094.012.	SEQ	ID	NO:	822	is	the	determined	cDNA	sequence	for	clone
	R0094:H01.										6	,
	D0004 1102	SEQ	ID	NO:	823	İS	the	determined	cDNA	sequence	tor	clone
	R0094:H03.	SEO	מז	NO.	824	ic	tha	determined	cDNA	ceanence	for	clone
10	R0094:H04.	удс	ענו	NO.	024	12	uic	determined	CDNA	sequence	101	Cione
10	1007.1110.11	SEQ	ID	NO:	825	is	the	determined	cDNA	sequence	for	clone
	R0094:H05.									_	•	
		SEQ	ID	NO:	826	is	the	determined	cDNA	sequence	for	clone
	R0094:H06.											
15		SEQ	ID	NO:	827	is	the	determined	cDNA	sequence	for	clone
	R0094:H08.											•
	D0004-1100	SEQ	ID	NO:	828	15	the	determined	cDNA	sequence	for	clone
	R0094:H09.	SEO		NO.	829	is	the	determined	cDNA	sequence	for	clone
20	R0094:H10.	DEQ	ענ	110.	027	15	шо	dotorminod	CDIVII	ooquonoo	101	010110
		SEQ	ID	NO:	830	is	the	determined	cDNA	sequence	for	clone
	R0094:H11.						1					
		SEQ	ID	NO:	831	is	the	determined	cDNA	sequence	for	clone
	R0095:A03.											
25		SEQ	ID	NO:	832	is	the	determined	cDNA	sequence	for	clone
	R0095:A06.	270	**	3.70					D.7.1		C	
	D0005.407	SEQ	ID ·	NO:	833	18	the	determined	cDNA	sequence	ior	clone
	R0095:A07.	SEO	מו	NO.	834	ic	the	determined	cDN4	segmence	for	clone
30	R0095:B01.	טבע	ענ	110.	027	10	uic	dotoffiffied	SIDI 111	Doquono	101	CIOILO
- •		SEQ	ID	NO:	835	is	the	determined	cDNA	sequence	for	clone

R0095:B02. SEQ ID NO: 836 is the determined cDNA sequence for clone R0095:B03. SEQ ID NO: 837 is the determined cDNA sequence for clone R0095:B04. SEQ ID NO: 838 is the determined cDNA sequence for clone R0095:B05. SEQ ID NO: 839 is the determined cDNA sequence for clone R0095:B06. SEQ ID NO: 840 is the determined cDNA sequence for clone 10 R0095:B10. SEQ ID NO: 841 is the determined cDNA sequence for clone R0095:B11. SEQ ID NO: 842 is the determined cDNA sequence for clone R0095:B12. SEQ ID NO: 843 is the determined cDNA sequence for clone R0095:C01. SEQ ID NO: 844 is the determined cDNA sequence for clone R0095:C03. SEQ ID NO: 845 is the determined cDNA sequence for clone 20 R0095:C04. SEQ ID NO: 846 is the determined cDNA sequence for clone R0095:C05. SEQ ID NO: 847 is the determined cDNA sequence for clone R0095:C06. 25 SEQ ID NO: 848 is the determined cDNA sequence for clone R0095:C07. SEQ ID NO: 849 is the determined cDNA sequence for clone R0095:C08. SEQ ID NO: 850 is the determined cDNA sequence for clone 30 R0095:C10.

	D0005.C12	SEQ	ID	NO:	851	is	the	determined	cDNA	sequence	for	clone
	R0095:C12.	SEQ	ID	NO:	852	is	the	determined	cDNA	sequence	for	clone
5	R0095:D01.	SEQ	ID	NO:	853	is	the	determined	cDNA	sequence	for	clone
	R0095:D03.									•		
	R0095:D04.	SEQ	ID	NO:	854	is	the	determined	cDNA	sequence	for	clone
10	R0095:D06.	SEQ	ID	NO:	855	is	the	determined	cDNA	sequence	for	clone
10	10073.200.	SEQ	ID	NO:	856	is	the	determined	cDNA	sequence	for	clone
	R0095:D07.	SEQ	ID	NO:	857	is	the	determined	cDNA	sequence	for	clone
15	R0095:D08.	SEO	ID	NO:	050	:.	tha	determined	aDNIA	gagyanaa	for	alana
13	R0095:D09.	SEQ	ענ	NO.	020	12	ше	determined	CDIVA	sequence	101	clone
	R0095:D11.	SEQ	ID	NO:	859	is	the	determined	cDNA	sequence	for	clone
20	R0095:D12.	SEQ	ID	NO:	860	is	the	determined	cDNA	sequence	for	clone
20	K0093.D12.	SEQ	ID	NO:	861	is	the	determined	cDNA	sequence	for	clone
	R0095:E01.	SEQ	ID	NO:	862	is	the	determined	cDNA	sequence	for	clone
	R0095:E02.									_		
25	R0095:E04.	SEQ	עו	NO:	863	15	the	determined	cDNA	sequence	ior	clone
	R0095:E05.	SEQ	ID	NO:	864	is	the	determined	cDNA	sequence	for	clone
		SEQ	ID	NO:	865	is	the	determined	cDNA	sequence	for	clone
30	R0095:E06.	SEQ	ID	NO:	866	is	the	determined	cDNA	sequence	for	clone

R0095:E07. SEQ ID NO: 867 is the determined cDNA sequence for clone R0095:E08. SEQ ID NO: 868 is the determined cDNA sequence for clone R0095:E11. SEQ ID NO: 869 is the determined cDNA sequence for clone R0095:E12. SEQ ID NO: 870 is the determined cDNA sequence for clone R0095:F01. SEQ ID NO: 871 is the determined cDNA sequence for clone 10 R0095:F03. SEQ ID NO: 872 is the determined cDNA sequence for clone R0095:F06. SEQ ID NO: 873 is the determined cDNA sequence for clone R0095:F10. SEQ ID NO: 874 is the determined cDNA sequence for clone R0095:F11. SEQ ID NO: 875 is the determined cDNA sequence for clone R0095:G02. SEQ ID NO: 876 is the determined cDNA sequence for clone 20 R0095:G03. SEQ ID NO: 877 is the determined cDNA sequence for clone R0095:G04. SEQ ID NO: 878 is the determined cDNA sequence for clone R0095:G08. 25 SEQ ID NO: 879 is the determined cDNA sequence for clone R0095:G09. SEQ ID NO: 880 is the determined cDNA sequence for clone R0095:G10. SEQ ID NO: 881 is the determined cDNA sequence for clone 30 R0095:H01.

SEQ ID NO: 882 is the determined cDNA sequence for clone R0095:H02. SEQ ID NO: 883 is the determined cDNA sequence for clone R0095:H04. SEQ ID NO: 884 is the determined cDNA sequence for clone 5 R0095:H06. SEQ ID NO: 885 is the determined cDNA sequence for clone R0095:H07. SEQ ID NO: 886 is the determined cDNA sequence for clone R0095:H09. 10 SEQ ID NO: 887 is the determined cDNA sequence for clone R0096:A02. SEQ ID NO: 888 is the determined cDNA sequence for clone R0096:A08. SEQ ID NO: 889 is the determined cDNA sequence for clone 15 R0096:A09. SEO ID NO: 890 is the determined cDNA sequence for clone R0096:A10. SEQ ID NO: 891 is the determined cDNA sequence for clone R0096:A11. SEQ ID NO: 892 is the determined cDNA sequence for clone R0096:A12. SEQ ID NO: 893 is the determined cDNA sequence for clone R0096:B02. SEQ ID NO: 894 is the determined cDNA sequence for clone 25 R0096:B03. SEQ ID NO: 895 is the determined cDNA sequence for clone R0096:B04. SEQ ID NO: 896 is the determined cDNA sequence for clone R0096:B05. 30 SEQ ID NO: 897 is the determined cDNA sequence for clone

R0096:B06. SEQ ID NO: 898 is the determined cDNA sequence for clone R0096:B07. SEQ ID NO: 899 is the determined cDNA sequence for clone R0096:B08. SEQ ID NO: 900 is the determined cDNA sequence for clone R0096:B09. SEQ ID NO: 901 is the determined cDNA sequence for clone R0096:B10. SEQ ID NO: 902 is the determined cDNA sequence for clone 10 R0096:B11. SEQ ID NO: 903 is the determined cDNA sequence for clone R0096:B12. SEQ ID NO: 904 is the determined cDNA sequence for clone R0096:C01. 15 SEQ ID NO: 905 is the determined cDNA sequence for clone R0096:C03. SEQ ID NO: 906 is the determined cDNA sequence for clone R0096:C04. SEQ ID NO: 907 is the determined cDNA sequence for clone 20 R0096:C05. SEQ ID NO: 908 is the determined cDNA sequence for clone R0096:C06. SEQ ID NO: 909 is the determined cDNA sequence for clone R0096:C07. 25 SEQ ID NO: 910 is the determined cDNA sequence for clone R0096:C08. SEQ ID NO: 911 is the determined cDNA sequence for clone R0096:C09. SEQ ID NO: 912 is the determined cDNA sequence for clone 30 R0096:C10.

	•	SEO	ID	NO:	913	is	the	determined	cDNA	sequence	for	clone
	R0096:C11.	~~~			,,,					204		
		SEQ	ID	NO:	914	is	the	determined	cDNA	sequence	for	clone
	R0096:C12.								•	-		
5		SEQ	ID	NO:	915	is	the	determined	cDNA	sequence	for	clone
	R0096:D01.										•	
		SEQ	ID	NO:	916	is	the	determined	cDNA	sequence	for	clone
ì	R0096:D02.	ar.o		270	015				73.74		6	
10	R0096:D03.	SEQ	ID	NO:	917	1S	the	determined	cDNA	sequence	tor	clone
10	K0030.D03.	SEO	ΙD	NO.	918	is	the	determined	cDNA	sequence:	for	clone
	R0096:D04.	محر	10	110.	710	,,,	tho	dottillimod	ODIVII	ooquonoo		. 010110
		SEQ	ID	NO:	919	is	the	determined	cDNA	sequence	for	clone
	R0096:D05.											
15		SEQ	ID	NO:	920	is	the	determined	cDNA	sequence	for	clone
	R0096:D08.											
	D0006 D00	SEQ	ID	NO:	921	is	the	determined	cDNA	sequence	for	clone
	R0096:D09.	SEO	ID	NO:	022	ic	the	determined	cDNA	caguence	for	clone
20	R0096:D10.	bLQ	ענו	110.	722	15	tHC	·	CDNA	sequence	101	CIOIIC
		SEQ	ID	NO:	923	is	the	determined	cDNA	sequence	for	clone
	R0096:D12.									_		
		SEQ	ID	NO:	924	is	the	determined	cDNA	sequence	for	clone
	R0096:E01.											
25		SEQ	ID	NO:	925	is	the	determined	cDNA	sequence	for	clone
	R0096:E02.	~~~		3.70								_
	D0006-E02	SEQ	ID	NO:	926	18	the	determined	cDNA	sequence	for	clone
	R0096:E03.	SEO	תו	NO.	927	ie	the	determined	cDNA	seguence	for	clone
30	R0096:E04.	or d	٠.	110.	121	19	uic	dottermined	ODINA	sequence	101	CIONE
- *	2 2 2 2 3	SEQ	ID	NO:	928	is	the	determined	cDNA	sequence	for	clone
		•							•	•		

R0096:E05. SEQ ID NO: 929 is the determined cDNA sequence for clone R0096:E06. SEQ ID NO: 930 is the determined cDNA sequence for clone R0096:E08. SEQ ID NO: 931 is the determined cDNA sequence for clone R0096:E09. SEQ ID NO: 932 is the determined cDNA sequence for clone R0096:E10. SEQ ID NO: 933 is the determined cDNA sequence for clone 10 R0096:E11. SEQ ID NO: 934 is the determined cDNA sequence for clone R0096:E12. SEQ ID NO: 935 is the determined cDNA sequence for clone R0096:F01. 15 SEQ ID NO: 936 is the determined cDNA sequence for clone R0096:F02. SEQ ID NO: 937 is the determined cDNA sequence for clone R0096:F03. SEQ ID NO: 938 is the determined cDNA sequence for clone 20 R0096:F04. SEQ ID NO: 939 is the determined cDNA sequence for clone R0096:F05. SEQ ID NO: 940 is the determined cDNA sequence for clone R0096:F07. 25 SEQ ID NO: 941 is the determined cDNA sequence for clone R0096:F10. SEQ ID NO: 942 is the determined cDNA sequence for clone R0096:F11. SEQ ID NO: 943 is the determined cDNA sequence for clone 30 R0096:G01.

SEQ ID NO: 944 is the determined cDNA sequence for clone R0096:G03. SEQ ID NO: 945 is the determined cDNA sequence for clone R0096:G04. SEQ ID NO: 946 is the determined cDNA sequence for clone 5, R0096:G05. SEQ ID NO: 947 is the determined cDNA sequence for clone R0096:G06. SEQ ID NO: 948 is the determined cDNA sequence for clone R0096:G07. 10 SEQ ID NO: 949 is the determined cDNA sequence for clone R0096:G09. SEQ ID NO: 950 is the determined cDNA sequence for clone R0096:G10. 15 SEQ ID NO: 951 is the determined cDNA sequence for clone R0096:G12. SEQ ID NO: 952 is the determined cDNA sequence for clone R0096:H01. SEQ ID NO: 953 is the determined cDNA sequence for clone R0096:H02. 20 SEQ ID NO: 954 is the determined cDNA sequence for clone R0096:H03. SEQ ID NO: 955 is the determined cDNA sequence for clone R0096:H07. SEQ ID NO: 956 is the determined cDNA sequence for clone 25 R0096:H08. SEQ ID NO: 957 is the determined cDNA sequence for clone R0097:A05. SEQ ID NO: 958 is the determined cDNA sequence for clone R0097:A06. 30 SEQ ID NO: 959 is the determined cDNA sequence for clone

R0097:A10. SEQ ID NO: 960 is the determined cDNA sequence for clone R0097:A11. SEQ ID NO: 961 is the determined cDNA sequence for clone R0097:B01. SEQ ID NO: 962 is the determined cDNA sequence for clone R0097:B03. SEQ ID NO: 963 is the determined cDNA sequence for clone R0097:B04. SEQ ID NO: 964 is the determined cDNA sequence for clone 10 R0097:B05. SEQ ID NO: 965 is the determined cDNA sequence for clone R0097:B06. SEQ ID NO: 966 is the determined cDNA sequence for clone R0097:B07. SEQ ID NO: 967 is the determined cDNA sequence for clone R0097:B11. SEQ ID NO: 968 is the determined cDNA sequence for clone R0097:C01. SEQ ID NO: 969 is the determined cDNA sequence for clone 20 R0097:C02. SEQ ID NO: 970 is the determined cDNA sequence for clone R0097:C03. SEQ ID NO: 971 is the determined cDNA sequence for clone R0097:C04. 25 SEQ ID NO: 972 is the determined cDNA sequence for clone R0097:C05. SEQ ID NO: 973 is the determined cDNA sequence for clone R0097:C07. SEQ ID NO: 974 is the determined cDNA sequence for clone 30 R0097:C08.

R0097:C09. SEQ ID NO: 976 is the determined cDNA sequence for clone R0097:D01. SEQ ID NO: 977 is the determined cDNA sequence for clone R0097:D01. SEQ ID NO: 978 is the determined cDNA sequence for clone R0097:D08. SEQ ID NO: 979 is the determined cDNA sequence for clone R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 983 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 984 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 984 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 984 is the determined cDNA sequence for clone R0097:F01. SEQ ID NO: 984 is the determined cDNA sequence for clone R0097:F01. S	quence for clone	cDNA	determined	the	is	975	NO:	ΙĎ	SEQ		
R0097:C10. SEQ ID NO: 977 is the determined cDNA sequence for clone R0097:D01. SEQ ID NO: 978 is the determined cDNA sequence for clone R0097:D08. SEQ ID NO: 979 is the determined cDNA sequence for clone R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.										R0097:C09.	
SEQ ID NO: 977 is the determined cDNA sequence for clone R0097:D01. SEQ ID NO: 978 is the determined cDNA sequence for clone R0097:D08. SEQ ID NO: 979 is the determined cDNA sequence for clone R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.	quence for clone	cDNA	determined	the	is	976	NO:	ID	SEQ		
R0097:D01. SEQ ID NO: 978 is the determined cDNA sequence for clone R0097:D08. SEQ ID NO: 979 is the determined cDNA sequence for clone R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.					٠					R0097:C10.	
SEQ ID NO: 978 is the determined cDNA sequence for clone R0097:D08. SEQ ID NO: 979 is the determined cDNA sequence for clone R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.	quence for clone	cDNA	determined	the	is	977	NO:	ID	SEQ		5
R0097:D08. SEQ ID NO: 979 is the determined cDNA sequence for clone R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.										R0097:D01.	
SEQ ID NO: 979 is the determined cDNA sequence for clone R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.	quence for clone	cDNA	determined	the	is	978	NO:	ID	SEQ		
R0097:E02. SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.										R0097:D08.	
SEQ ID NO: 980 is the determined cDNA sequence for clone R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.	quence for clone	cDNA	determined	the	is	979	NO:	ID	SEQ		
R0097:E09. SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.										R0097:E02.	10
SEQ ID NO: 981 is the determined cDNA sequence for clone R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.	quence for clone	cDNA	determined	the	is	980	NO:	ID	SEQ		
R0097:E11. SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.				-						R0097:E09.	
SEQ ID NO: 982 is the determined cDNA sequence for clone R0097:F01.	quence for clone	cDNA	determined	the	is	981	NO:	ID	SEQ		
R0097:F01.									~~~	R0097:E11.	
	quence for clone	cDNA	determined	the	15	982	NO:	ID	SEQ	D0007 F01	15
SEQ ID NO: 983 is the determined cDNA sequence for clone		-TDN [A	1.4	41	•	002	NO	m	GEO.	K009/:F01.	
R0097:F11.	quence for clone	CDNA	determined	ine	15	983	NO:	ענ	SEQ	D0007-E11	
SEQ ID NO: 984 is the determined cDNA sequence for clone	guanga for along	•DNI A	determined	tha	i o	084	NO.	ID	SEO	K0097.F11.	
20 R0097:G01.	duetice tot cione	CDIVA	determined	ще	15	704	110.	ענו	BEQ	R0097:G01	20
SEQ ID NO: 985 is the determined cDNA sequence for clone	quence for clone	cDNA	determined	the	is	985	NO.	ΙD	SEO	10077.001.	20
R0097:G11.	quence for eleme	001171	dotolilliod	uio	15	705	110.	110	DLQ	R0097:G11.	
SEQ ID NO: 986 is the determined cDNA sequence for clone	quence for clone	cDNA	determined	the	is	986	NO:	ID	SEO	2000,	
R0097:G12.						,				R0097:G12.	
SEQ ID NO: 987 is the determined cDNA sequence for clone	quence for clone	cDNA	determined	the	is	987	NO:	ID	SEQ		25
R0097:H01.	•	•		•						R0097:H01.	
SEQ ID NO: 988 is the determined cDNA sequence for clone	quence for clone	cDNA	determined	the	is	988	NO:	ID	SEQ		
R0097:H02.										R0097:H02.	
SEQ ID NO: 989 is the determined cDNA sequence for clone	quence for clone	cDNA	determined	the	is	989	NO:	ID	SEQ		
30 R0097:H04.										R0097:H04.	30
SEQ ID NO: 990 is the determined cDNA sequence for clone	quence for clone	cDNA	determined	the	is	990	NO:	ID	SEQ		

R0097:H06. SEQ ID NO: 991 is the determined cDNA sequence for clone R0097:H07. SEQ ID NO: 992 is the determined cDNA sequence for clone R0097:H09. SEQ ID NO: 993 is the determined cDNA sequence for clone R0097:H11. SEQ ID NO: 994 is the determined cDNA sequence for clone R0098:A03. SEQ ID NO: 995 is the determined cDNA sequence for clone 10 R0098:A05. SEQ ID NO: 996 is the determined cDNA sequence for clone R0098:A06. SEQ ID NO: 997 is the determined cDNA sequence for clone R0098:A10. SEQ ID NO: 998 is the determined cDNA sequence for clone R0098:A12. SEQ ID NO: 999 is the determined cDNA sequence for clone R0098:B01. SEQ ID NO: 1000 is the determined cDNA sequence for clone 20 R0098:B02. SEQ ID NO: 1001 is the determined cDNA sequence for clone R0098:B05. SEQ ID NO: 1002 is the determined cDNA sequence for clone R0098:B06. 25 SEQ ID NO: 1003 is the determined cDNA sequence for clone R0098:B10. SEQ ID NO: 1004 is the determined cDNA sequence for clone R0098:C03. SEQ ID NO: 1005 is the determined cDNA sequence for clone 30 R0098:C04.

		SEQ	ID	NO:	1006	is	the	determined	cDNA	sequence	for	clone
	R0098:C05.	geo.	ID	NO.	1007	:	4l- a		a DNI A		for	alama
	R0098:C10.	SEQ	ענ	NO:	1007	15	tne	determined	CDNA	sequence	юг	CIONE
5		SEQ	ID	NO:	1008	is	the	determined	cDNA	sequence	for	clone
	R0098:C11.	SEO	ID	NO:	1009	is	the	determined	cDNA	sequence	for	clone
	R0098:D01.									1		
10	R0098:D02.	SEQ	ID	NO:	1010	is	the	determined	cDNA	sequence	for	clone
10	10076.D02.	SEQ	ID	NO:	1011	is	the	determined	cDNA	sequence	for	clone
	R0098:D07.	ano	TD	210	1010	•	.1		D) ()		C	,
	R0098:D08.	SEQ	ID	NU:	1012	18	the	determined	cDNA	sequence	ior	clone
15		SEQ	ID	NO:	1013	is	the	determined	cDNA	sequence	for	clone
	R0098:D09.	SEQ	ID	NO:	1014	is	the	determined	cDNA	sequence	for	clone
	R0098:D10.									•		
20	R0098:D11.	SEQ	ID	NO:	1015	is	the	determined	cDNA	sequence	for	clone
20	11005,0.211.	SEQ	ID	NO:	1016	is	the	determined	cDNA	sequence	for	clone
	R0098:D12.	gr.o	ıD	NO.	1017	:	41		-DNIA		£	
	R0098:E01.	SEQ	ענ	NO:	1017	18	me	determined	CDNA	sequence	101	cione
25		SEQ	ID	NO:	1018	is	the	determined	cDNA	sequence	for	clone
	R0098:E04.	SEQ	ID	NO:	1019	is	the	determined	cDNA	sequence	for	clone
	R0098:E05.									•		
30	R0098:E06.	SEQ	ID	NO:	1020	is	the	determined	cDNA	sequence	for	clone
50	TOO O. DOO.	SEQ	ID	NO:	1021	is	the	determined	cDNA	sequence	for	clone

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R0098:E07. SEQ ID NO: 1022 is the determined cDNA sequence for clone R0098:E11. SEQ ID NO: 1023 is the determined cDNA sequence for clone R0098:F04. SEQ ID NO: 1024 is the determined cDNA sequence for clone R0098:F05. SEQ ID NO: 1025 is the determined cDNA sequence for clone R0098:F06. SEQ ID NO: 1026 is the determined cDNA sequence for clone 10 R0098:F07. SEQ ID NO: 1027 is the determined cDNA sequence for clone R0098:F08. SEQ ID NO: 1028 is the determined cDNA sequence for clone R0098:F09. 15 SEQ ID NO: 1029 is the determined cDNA sequence for clone R0098:F10. SEQ ID NO: 1030 is the determined cDNA sequence for clone R0098:F11: SEQ ID NO: 1031 is the determined cDNA sequence for clone 20 R0098:F12. SEQ ID NO: 1032 is the determined cDNA sequence for clone R0098:G02. SEQ ID NO: 1033 is the determined cDNA sequence for clone R0098:G03. 25 SEQ ID NO: 1034 is the determined cDNA sequence for clone R0098:G05. SEQ ID NO: 1035 is the determined cDNA sequence for clone R0098:G06. SEQ ID NO: 1036 is the determined cDNA sequence for clone 30 R0098:G07.

		SEQ	ID	NO:	1037	is	the	determined	cDNA	sequence	for	clone
	R0098:G08.										•	
		SEQ	ID	NO:	1038	is	the	determined	cDNA	sequence	for	clone
	R0098:G09.										0	,
5	70000 010	SEQ	ID	NO:	1039	is	the	determined	cDNA	sequence	tor	cione
	R0098:G10.	ar.	т	210	1040		.1	1.4	~T)\\ I A		£	alama
	D0000.C11	SEQ	Ш.	NO:	1040	15	tne	determined	CDNA	sequence	101	cione
	R0098:G11.	SEO	תו	NO.	1041	ic	the	determined	cDNA	seguence	for	clone
10	R0098:G12.	brQ	Λti	110.	1071	12	шс	determined	CDIVI	sequence	101	CIONO
	10070.012.	SEO	ID	NO:	1042	is	the	determined	cDNA	sequence	for	clone
	R0098:H02.			•						•		
		SEQ	ID	NO:	1043	is	the	determined	cDNA	sequence	for	clone
	R0098:H03.											
15		SEQ	ID	NO:	1044	is	the	determined	cDNA	sequence	for	clone
	R0098:H04.											
		SEQ	ID	NO:	1045	is	the	determined	cDNA	sequence	for	clone
	R0098:H05.											
		SEQ	ID	NO:	1046	is	the	determined	cDNA	sequence	for	clone
20	R0098:H07.	~=~					.•		D) I I		c	1
	D0000 1100	SEQ	ID	NO:	1047	18	the	determined	cDNA	sequence	ior	clone
	R0098:H08.	SEO.	ID	NO.	1049	ia	tha	determined	aDNA.	ceguence	for	clone
	R0098:H11.	BEQ	עו	NO.	1040	12	ше	determined	CDNA	sequence	101	CIOIIC
25	K0098.III1.	SEO	ו מו	VO: 1	049 is	the	dete	ermined cDN	A seane	ence for clo	one (C878P
	which shows	`							•			
	NT2RP40019:	, ~			•			-				
				-				l cDNA sequ				
	shows sequen	ce sim	ilari	ity to	homo	sap	iens	cDNA FLJ2	20116 fi	s, clone C	OLC	5655

and homo sapiens cDNA FLJ20740 fis, clone HEP07118.

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SEQ ID NO: 1051 is the determined cDNA sequence for clone C883P which shows sequence similarity to human homeobox protein Cdx2 mRNA.

SEQ ID NO: 1052 is the determined cDNA sequence for clone C884P which shows sequence similarity to human TM4SF3 (aka, CO-029).

SEQ ID NO: 1053 is the determined cDNA sequence for clone C886P which shows sequence similarity to human secretory protein (P1.B) mRNA and homo sapiens trefoil factor 3 (intestinal) (TFF3) mRNA.

SEQ ID NO: 1054 is the determined cDNA sequence for clone C892P which shows sequence similarity to human galectin-4 mRNA.

SEQ ID NO: 1055 is the determined cDNA sequence for clone C900P which shows sequence similarity to homo sapiens mucin 11 (MUC11) mRNA.

SEQ ID NO: 1056 is the determined cDNA sequence for clone C902P which shows sequence similarity to homo sapiens calcium-dependent chloride channel-1 (hCLCA1) mRNA.

SEQ ID NO: 1057 is the determined cDNA sequence for clone C903P which shows sequence similarity to homo sapiens transmembrane mucin 12 (MUC12) mRNA.

SEQ ID NO: 1058 is the determined cDNA sequence for clone C899P which shows sequence similarity to homo sapiens intestinal mucin (MUC2) mRNA.

SEQ ID NO:1059 is the predicted amino acid sequence for the clone of SEQ ID NO:1049.

SEQ ID NO:1060 is the predicted amino acid sequence for the clone of SEQ ID NO:1050.

SEQ ID NO:1061 is the predicted amino acid sequence for the clone of SEQ ID NO:1051.

SEQ ID NO:1062 is the predicted amino acid sequence for the clone of SEQ ID NO:1052.

SEQ ID NO:1063 is the predicted amino acid sequence for the clone of SEQ ID NO:1053.

SEQ ID NO:1064 is the predicted amino acid sequence for the clone of SEQ ID NO:1054.

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SEQ ID NO:1065 is the predicted amino acid sequence for the clone of SEQ ID NO:1055.

SEQ ID NO:1066 is the predicted amino acid sequence for the clone of SEQ ID NO:1056.

SEQ ID NO:1067 is the predicted amino acid sequence for the clone of SEQ ID NO:1057.

SEQ ID NO:1068 is the predicted amino acid sequence for the clone of SEQ ID NO:1058.

SEQ ID NO:1069 is the full length nucleotide sequence for clone CS1-152 (C880P, C887P).

SEQ ID NO:1070 is the predicted amino acid sequence for the clone of SEQ ID NO:1069.

SEQ ID NO:1071 is the cDNA sequence for human colon specific gene (geneseq X03195) identified from a computer search of the public geneseq database and which shows similarity to clone C880P.

SEQ ID NO:1072 is the cDNA sequence for human protein comprising secretory signal nucleotide sequence 3 (geneseq V29035) identified from a computer search of the public geneseq database and which shows similarity to clone C880P.

SEQ ID NO:1073 is the cDNA sequence for open reading frame human protein comprising secretory signal 3 (geneseq V29036) identified from a computer search of the public geneseq database and which shows similarity to clone C880P.

SEQ ID NO:1074 is the cDNA sequence for human colon specific protein cDNA (geneseq T51784) identified from a computer search of the public geneseq database and which shows similarity to clone C880P.

SEQ ID NO:1075 is the cDNA sequence for human Reg 1-gamma protein (geneseq V29156) identified from a computer search of the public geneseq database and which shows similarity to clone C880P.

SEQ ID NO:1076 is the cDNA sequence for human intestinal peptide-associated transporter HPT-1 mRNA, complete cds and homo sapiens mRNA for L1-cadherin (geneseq X18166) identified from a computer search of the public geneseq database and which shows similarity to clone C888P.

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SEQ ID NO:1077 is the amino acid sequence of geneseq record W12691 which shows sequence similarity to clone C880P.

SEQ ID NO:1078 is the amino acid sequence of geneseq record W37866 which shows sequence similarity to clone C880P.

SEQ ID NO:1079 is the amino acid sequence of geneseq record W37929 which shows sequence similarity to clone C880P.

SEQ ID NO:1080 is the amino acid sequence of geneseq record W84274 which shows sequence similarity to clone C880P.

SEQ ID NO:1081 is the amino acid sequence of geneseq record W740898 which shows sequence similarity to clone C888P.

SEQ ID NO:1082 is the determined cDNA sequence for clone 27540

SEQ ID NO:1083 is the predicted amino acid sequence of clone 27540 (SEQ ID NO:1082)

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as colon cancer. The compositions described herein may include colon tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a colon tumor protein or a variant thereof. A "colon tumor protein" is a protein that is expressed in colon tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain colon tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with colon cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above.

Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human colon tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081.

COLON TUMOR PROTEIN POLYNUCLEOTIDES

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Any polynucleotide that encodes a colon tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a colon tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a colon tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a colon tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity

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to a polynucleotide sequence that encodes a native colon tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) CABIOS 5:151-153; Myers, E.W. and Muller W. (1988) CABIOS 4:11-17; Robinson, E.D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference

sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native colon tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that is at least two fold greater in a colon tumor than in normal tissue, as determined

using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., Proc. Natl. Acad. Sci. USA 93:10614-10619, 1996 and Heller et al., Proc. Natl. Acad. Sci. USA 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as colon tumor cells. polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a colon tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

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For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ³²P) using well known techniques. bacterial or bacteriophage library is then screened by hybridizing filters containing 20 denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

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Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

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One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al., Nucl. Acids Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding portions of colon tumor proteins are provided in SEQ ID NO: 1-121, 123-197, 205-630, 632-684, 686, 690-691, and 694-1081. These polynucleotides were isolated from colon tumor cDNA libraries using conventional and/or PCR-based subtraction techniques, as described below.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding a colon tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a colon tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

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A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability in vivo. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetylmethyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

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Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally

transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (i.e., an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

COLON TUMOR POLYPEPTIDES

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Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a colon tumor protein or a variant thereof, as described herein. As noted above, a "colon tumor protein" is a protein that is expressed by colon tumor cells. Proteins that are colon tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with colon cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a colon tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigenspecific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native colon tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

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As noted above, a composition may comprise a variant of a native colon tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native colon tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigenspecific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants

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in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Α Preferably, a variant contains conservative substitutions. "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain non-conservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

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Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

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Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both

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immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

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Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., Gene 40:39-46, 1985; Murphy et al., Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino

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acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

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Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene 43*:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible

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for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology 10*:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

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The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a colon tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a colon tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a colon tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about

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10³ L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as colon cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a colon tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin

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or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, Eur. J. Immunol. 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

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Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be

prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl

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groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing

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nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

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T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a colon tumor protein. Such cells may generally be prepared in vitro or ex vivo, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA. Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a colon tumor polypeptide, polynucleotide encoding a colon tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a colon tumor polypeptide or polynucleotide is 25 present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a colon tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation,

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compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a colon tumor polypeptide (100 ng/ml - 100 µ g/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-y) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a colon tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Colon tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a colon tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a colon tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a colon tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a colon tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

30 PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or

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binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (i.e., vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable Vaccines may comprise one or more such compounds and an carrier. immunostimulant. An immunostimulant may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

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A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated in situ. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, Crit. Rev. Therap. Drug Carrier Systems 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., Proc. Natl. Acad. Sci. USA 86:317-321, 1989; Flexner et al., Ann. N.Y.

Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., Proc. Natl. Acad. Sci. USA 91:215-219, 1994; Kass-Eisler et al., Proc. Natl. Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

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Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present

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invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bortadella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

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Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, TNFα, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, Ann. Rev. Immunol. 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type.

30 response include, for example, a combination of monophosphoryl lipid A, preferably

3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.

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MPL adjuvants are available from Corixa Corp. (Seattle, WA) (see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences are also described, for example, by Sato et al., Science 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc., Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

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Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (e.g., SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Corixa, Seattle, WA) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (see, e.g. Coombes et al., Vaccine 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained

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within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-coglycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (e.g., a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (see e.g., U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their

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ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells in vivo or ex vivo, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., Nature Med. 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcγ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a colon tumor protein (or portion or other variant thereof) such that the colon tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising

such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the colon tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unitdose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

CANCER THERAPY

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In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as colon cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor.

Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

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Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic,

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macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term in vivo. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., Immunological Reviews 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated ex vivo for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

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Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccinedependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to nonvaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a colon tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

15 METHODS FOR DETECTING CANCER

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In general, a cancer may be detected in a patient based on the presence of one or more colon tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as colon cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a colon tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b)

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detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent. Suitable polypeptides for use within such assays include full length colon tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding

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agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

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More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (i.e., incubation time) is a period of time that is sufficient to detect the

presence of polypeptide within a sample obtained from an individual with colon cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20[™]. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibodypolypeptide complex for an amount of time sufficient to detect the bound polypeptide.

An appropriate amount of time may generally be determined by assaying the level of
binding that occurs over a period of time. Unbound detection reagent is then removed
and bound detection reagent is detected using the reporter group. The method
employed for detecting the reporter group depends upon the nature of the reporter
group. For radioactive groups, scintillation counting or autoradiographic methods are
generally appropriate. Spectroscopic methods may be used to detect dyes,
luminescent groups and fluorescent groups. Biotin may be detected using avidin,
coupled to a different reporter group (commonly a radioactive or fluorescent group or
an enzyme). Enzyme reporter groups may generally be detected by the addition of
substrate (generally for a specific period of time), followed by spectroscopic or other
analysis of the reaction products.

To determine the presence or absence of a cancer, such as colon cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered

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positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich

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assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use colon tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such colon tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a colon tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a colon tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with one or more representative polypeptides (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of colon tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

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As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a colon tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a colon tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e., hybridizes to) a polynucleotide encoding the colon tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a colon tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

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To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a colon tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-121, 123-197, 205-630, 632-684, 686, 690-691, and 694-1081. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and

from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple colon tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

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The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds,

reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a colon tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a colon tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a colon tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a colon tumor protein.

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The following Examples are offered by way of illustration and not by way of limitation.

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EXAMPLES

Example 1

ISOLATION AND CHARACTERIZATION OF COLON TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION AND MICROARRAY ANALYSIS

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A cDNA library was constructed in the PCR2.1 vector (Invitrogen, Carlsbad, CA) by subtracting a pool of three colon tumors with a pool of normal colon, spleen, brain, liver, kidney, lung, stomach and small intestine using PCR subtraction methodologies (Clontech, Palo Alto, CA). The subtraction was performed using a PCR-based protocol, which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs, and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are over-expressed in colon tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

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To characterize the complexity and redundancy of the subtracted library, 96 clones were randomly picked and 65 were sequenced, as previously described. These sequences were further characterized by comparison with the most recent Genbank database (April, 1998) to determine their degree of novelty. No significant homologies were found to 21 of these clones, hereinafter referred to as 11092, 11093, 11096, 11098, 11103, 11174, 11108, 11112, 11115, 11117, 11118, 11134, 11151, 11154, 11158, 11168, 11172, 11175, 11184, 11185 and 11187. The determined cDNA sequences for these clones are provided in SEQ ID NO: 48, 49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101 and 109-111, respectively.

Two-thousand clones from the above mentioned cDNA subtraction library were randomly picked and submitted to a round of PCR amplification. Briefly, 0.5 μl of glycerol stock solution was added to 99.5 μl of pcr MIX (80 μl H₂0, 10 μl 10X PCR Buffer, 6 μl 25 mM MgCl₂, 1 μl 10 mM dNTPs, 1 μl 100 mM M13 forward primer (CACGACGTTGTAAAACGACGG), 1 μl 100 mM M13 reverse primer (CACAGGAAACAGCTATGACC)), and 0.5 μl 5 u/ml Taq polymerase (primers provided by (Operon Technologies, Alameda, CA). The PCR amplification was run for thirty cycles under the following conditions: 95°C for 5 min., 92°C for 30 sec., 57°C for 40 sec., 75°C for 2 min. and 75°C for 5 minutes.

mRNA expression levels for representative clones were determined using microarray technology (Synteni, Palo Alto, CA) in colon tumor tissues (n=25), normal colon tissues (n=6), kidney, lung, liver, brain, heart, esophagus, small intestine, stomach, pancreas, adrenal gland, salivary gland, resting PBMC, activated

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PBMC, bone marrow, dendritic cells, spinal cord, blood vessels, skeletal muscle, skin, breast and fetal tissues. The number of tissue samples tested in each case was one (n=1), except where specifically noted above; additionally, all the above-mentioned tissues were derived from humans. The PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, and fluorescent-labeled cDNA probes were generated by reverse transcription according to the protocol provided by Synteni. The microarrays were probed with the labeled cDNA probes, the slides scanned, and fluorescence intensity was measured. This intensity correlates with the hybridization intensity.

One hundred and forty nine clones showed two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group. These cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). These sequences were compared to known sequences in the most recent GenBank database. No significant homologies to human gene sequences were found in forty nine of these clones, represented by the following sixteen cDNA consensus sequences: SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46 and 47, hereinafter referred to as Contig 2, 8, 13, 14, 20, 23, 29, 31, 35, 32, 36, 38, 41, 42, 50 and 51, respectively). Contig 29 (SEQ ID NO: 30) was found to be a Rat GSK-3-β-interacting protein Axil homolog. Also, Contigs 31 and 35 (SEQ ID NO: 32 and 33, respectively) were found to be a Mus musculus GOB-4 homolog. The determined cDNA sequences of SEQ ID NO: 1, 3-7, 9-14, 17-21, 23, 25-29, 31, 35, 37, 39, 42-45, 50, 51, 53, 55-58, 61-64, 70-78, 80-88, 91, 92, 94-98, 102-108 and 112 were found to show some homology to previously identified genes sequences.

Microarray analysis demonstrated Contig 2 (SEQ ID NO: 2) showed over-expression in 34% of colon tumors tested, as well as increased expression in normal pancreatic tissue, with no over-expression in normal colon tissues. Upon further analysis, Contigs 2, 8 and 23 were found to share homology to the known gene GW112. Contigs 4, 5, 9 and 52 showed homology to carcinoembryonic antigen (SEQ ID NO: 3, 4, 5 and 6, respectively). A representative sampling of these fragments

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showed over-expression in 85% of colon tumors, with over-expression in normal bone marrow and 3/6 normal colon tissues. Contig 6 (SEQ ID NO: 7), showing homology to the known gene sequence for villin, and was over-expressed in about half of all colon tumors tested, with a limited degree of low level over-expression in normal colon. Contig 12 (SEQ ID NO: 14), showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P, was over-expressed in approximately 70% of colon tumors tested, with low over-expression in 1/6 normal colon samples. Contig 14, also referred to as 14261 (SEQ ID NO: 16), showing no significant homology to any known gene, showed over-expression in 44% of colon tumors tested, with low level expression in half of normal colon tissues, as well as small intestine and pancreatic tissue. Contig 18 (SEQ ID NO: 21), showing homology to the known gene for L1-cadherin, showed over-expression in approximately half of colon tumors and low level over-expression in 3/6 normal colon tissues tested. Contig 22 (SEQ ID NO: 23), showing homology to Bumetanide-sensitive Na-K-Cl cotransporter was over-expressed in 70% of colon tumors and no over-expression in all normal tissues tested. Contig 25 (SEQ ID NO: 25), showing homology to macrophage inflammatory protein-3α, was over-expressed in over 40% of colon tumors and in activated PBMC. Contigs 26 and 48 (SEQ ID NOS: 25 and 26), showing homology to the sequence for laminin, was over-expressed in 48% of colon tumors and with low over-expression in stomach tissue. Contig 28 (SEQ ID NO: 29), showing homology to the known gene sequence for Chromosome 16 BAC clone CIT987SK-A-363E6, was over-expressed in 33% of colon tumors tested with normal stomach and 2/6 normal colon tissues showing low level over-expression. Contigs 29, 31 and 35 (SEQ ID NOS: 30, 32 and 33, respectively), also referred to as C751P, an unknown sequence showing limited and partial homology to Rat GSK-3\beta-interacting protein Axil homolog.and Mus musculus GOB-4 homolog, was over-expressed in 74% of colon tumors and no overexpression in all normal tissues tested. Contig 34 (SEQ ID NO: 35), showing homology to the known sequence for desmoglein 2, was over-expressed in 56% of colon tumors and showed low level over-expression in 1/6 normal colon tissues. Contig 36 (SEQ ID NO: 36), an unknown sequence also referred to as C793P, showed over-expression in 30% of colon tumor tissues tested. Contig 37 and 14287.2 (SEQ

ID NOS: 37 and 116), an unknown sequence, but with limited (89%) homology to the known sequence for putative transmembrane protein was over-expressed in 70% of colon tumors, as well as in normal lung tissue and 3/6 normal colon tissues tested. Contig 38, also referred to as C796P and 14219 (SEQ ID NO: 38), showing no significant homology to any known gene, was over-expressed in 38% in colon tumors and no elevated over-expression in any normal tissues. Contig 41 (SEQ ID NO: 40), also referred to as C799P and 14308, an unknown sequence showing no significant homology to any known gene, was over-expressed in 22% of colon tumors. Contig 42, (SEQ ID NO: 41), also referred to as C794P and 14309, an unknown sequence with no significant homology to any known gene, was over-expressed in 63% of colon tumors tested, as well as in 3/6 normal colon tissues. Contig 43 (SEQ ID NO: 42), showing homology to the known sequence for Chromosome 1 specific transcript KIAA0487 was over-expressed in 85% of colon tumors tested and in normal lung and 4/6 normal colon tissues. Contig 49 (SEQ ID NO: 45), showing homology to the known sequence for pump-1, was over-expressed in 44% of colon tumors and no over-expression in all normal tissues tested. Contig 50 (SEQ ID NO: 46), also referred to as C792P and 18323, showing no significant homology to any known gene, was over-expressed in 33% of colon tumors with no detectable over-expression in any normal tissues tested. Contig 51 (SEQ ID NO: 47), also referred to as C795P and 14317 was over-expressed in 11% of colon tumors.

Additional microarray analysis yielded seven clones showing two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group. Three of these clones demonstrated particularly good colon tumor specificity, and are represented by SEQ ID NO: 115, 116 and 120. Specifically, SEQ ID NO: 115, referred to as C791P or 14235, which shows homology to the known gene sequence for H. sapiens chromosome 21 derived BAC containing ets-2 gene, was over-expressed in 89% of colon tumors tested and in 5/6 normal colon tissues, as well as over-expressed at low levels in normal lung and activated PBMC. Microarray analysis for SEQ ID NO: 116 is discussed above. SEQ ID NO: 120, referred to as 14295, showing homology to the known gene sequence for secreted cement gland protein XAG-2 homolog, was over-expressed in 70% of colon tumors and in 5/6

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normal colon tissues, as well as low level over-expression in normal small intestine, stomach and lung. All clones showing over-expression in colon tumor were sequenced and these sequences compared to the most recent Genbank database (February 12, 1999). Of the seven clones, three contained sequences that did not share significant homology to any known gene sequences, represented by SEQ ID NO: 116, 117 and 119. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in colon. The determined cDNA sequences of the remaining clones (SEQ ID NO: 113-115 and 120) were found to show some homology to previously identified genes.

Further analysis identified a clone which was recovered several times by PCR subtraction and by expression screening using a mouse anti-scid antiserum. The determined full length cDNA sequence for this clone is provided in SEQ ID NO: 121, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 122. This clone is homologous with the known gene Beta IG-H3, as disclosed in U.S. Patent No. 5,444,164. Microarray analysis demonstrated this clone to be overexpressed in 75 to 80% of colon tumors tested (n=27), with no over-expression in normal colon samples (n=6), but with some low level over-expression in other normal tissues tested.

Further analysis of the PCR-subtraction library described above led to
the isolation of longer cDNA sequences for the clones of SEQ ID NO: 30, 115, 46,
118, 41, 47, 38, 113, 14 and 40 (known as C751P, C791P, C792P, C793P, C794P,
C795P, C796P, C797P, C798P and C799P, respectively). These determined cDNA
sequences are provided in SEQ ID NO: 123-132, respectively. Additional sequences
for the clones C794P and C799P are shown in SEQ ID NO:683 and 684, respectively,
and the predicted amino acid sequences are shown in SEQ ID NO:685 and 686,
respectively. Still further sequences for the clones C794P and C799P are shown in
SEQ ID NO: 691 and 690, respectively, and to the predicted amino acid sequence as
shown in SEQ ID NO: 693 and 692, respectively.

Using PCR subtraction methodology described above with minor modifications, transcripts from a pool of three moderately differentiated colon adenocarcinoma samples were subtracted with a set of transcripts from normal brain,

pancreas, bone marrow, liver, heart, lung, stomach and small intestine. Modifications of the above protocol were included at the cDNA digestion steps and in the tester to drive hybridization ratios. In a first subtraction, the restriction enzymes PvuII, DraI, MscI and StuI were used to digest cDNAs, and the tester to driver ratio was 1:40, as suggested by Clontech. In a second subtraction, DraI, MscI and StuI were used for cDNA digestion and a tester to driver ratio of 1:76 was used. Following the PCR amplification steps, the cDNAs were clones into pCR2.1 plasmid vector. determined cDNA sequences of 167 isolated clones are provided in SEQ ID NO: 205-These sequences were compared to sequences in the public databases as described above. The sequences of SEQ ID NO: 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369 and 371 were found to show some homology to previously identified ESTs. remaining sequences were found to show some homology to previously identified genes.

Using the PCR subtraction technology described above, a cDNA library from a pool of primary colon tumors was subtracted with a cDNA library prepared from normal tissues, including brain, bone marrow, kidney, heart, lung, liver, pancreas, small intestine, stomach and trachea. The determined cDNA sequences for 90 clones isolated in this subtraction are provided in SEQ ID NO: 372-461. Comparison of these sequences with those in the public databases as described above, revealed no homologies to the sequences of SEQ ID NO: 426, 445 and 453. The sequences of SEQ ID NO: 372-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455 and 457-461 showed some homology to previously identified genes, while the sequences of SEQ ID NO: 379, 405, 407, 408, 418, 424, 430-432, 437, 442, 444, 452 and 456 showed some homology to previously isolated ESTs.

Using the PCR subtraction methodology described above, a cDNA library prepared from a pool of metastatic colon tumors was subtracted with cDNA from a pool of normal tissues, namely brain, heart, lung, lymph nodes, PBMC,

pancreas, small intestine and stomach. The determined cDNA sequences for 82 clones isolated from the subtracted library are provided in SEQ ID NO: 487-568 (referred to as contigs 1-56 and 58-83, respectively). The sequences of SEQ ID NO: 487, 489, 490, 493-496, 499, 501-509, 511-518, 520-526, 529-542, 544, 546, 548-552, 554, 555, 557, 558, 560, 562, 563, 566 and 567 showed some homology to previously identified gene sequences. The sequences of SEQ ID NO: 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 559, 564, 564 and 568 showed some homology to previously isolated ESTs.

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Example 2

ISOLATION OF TUMOR POLYPEPTIDES USING SCID MOUSE-PASSAGED TUMOR RNA

Human colon tumor antigens were obtained using SCID mouse passaged colon tumor RNA as follows. Human colon tumor was implanted in SCID mice and harvested, as described in Patent Application Serial No. 08/556,659 filed 11/13/95, U.S. Patent No. 5,986,170. First strand cDNA was synthesized from poly A+ RNA from three SCID mouse-passaged colon tumors using a Lambda ZAP Express cDNA synthesis kit (Stratagene). The reactions were pooled and digested with RNase A, T1 and H to cleave the RNA and then treated with NaOH to degrade the RNA. The resulting cDNA was annealed with biotinylated (Vector Labs, Inc., Burlingame, CA) cDNA from a normal resting PBMC plasmid library (constructed from Superscript plasmid System, Gibco BRL), and subtracted with streptavidin by Second strand cDNA was synthesized from the phenol/chloroform extraction. subtracted first strand cDNA and digested with S1 nuclease (Gibco BRL). The cDNA was blunted with Pfu polymerase and EcoRI adaptors (Stratagene) were ligated to the ends. The cDNA was phosphorylated with T4 polynucleotide kinase, digested with restriction endonuclease XhoI, and size selected with Sephacryl S-400 (Sigma). Fractions were pooled, ligated to Lambda ZAP Express arms (Stratagene) and packaged with Gigapack Gold III extract (Stratagene). Random plaques were picked,

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phagemid was excised, transformed into XLOLR cells (Stratagene) and resulting plasmid DNA (Qiagen Inc., Valencia, CA) was sequenced as described above.

The determined cDNA sequences for 17 clones isolated as described above are provided in SEQ ID NO: 133-151, wherein 133 and 134 represent partial sequences of a clone referred to as CoSub-3 and SEQ ID NO: 135 and 136 represent partial sequences of a clone referred to as CoSub-13. These sequences were compared with those in the public databases as described above. The sequences of SEQ ID NO: 139 and 149 showed no significant homologies to any previously identified sequences. The sequences of SEQ ID NO: 138, 140, 141, 142, 143, 148 and 149 showed some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 133-137, 144-147, 150 and 151 showed some homology to previously isolated gene sequences.

The determined cDNA sequences for an additional 46 clones isolated as described above, are provided in SEQ ID NO: 569-616, wherein SEQ ID NO: 573 and 574 represent the 3' and 5' determined cDNA sequences, respectively, for clone CS1-106, and SEQ ID NO: 579 and 580 represent the determined 3' and 5' cDNA sequences, respectively, for clone CS1-124. Comparison of the isolated sequences with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 580, 585, 610 and 613. The sequences of SEQ ID NO: 569, 574-577, 584, 587, 592, 595, 598, 603 and 608 showed some homology to previously isolated ESTs, while the sequences of SEQ ID NO: 570-573, 578, 581-583, 586, 588-591, 593, 594, 596, 597, 599-602, 604-607, 609, 611, 612 and 514-616 showed some homology to previously isolated gene sequences.

Example 3

USE OF MOUSE ANTISERA TO IDENTIFY DNA SEQUENCES ENCODING COLON TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding colon tumor antigens by screening of colon tumor cDNA libraries with mouse antitumor sera.

. A cDNA expression library was prepared from SCID mouse-passaged

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human colon tumor poly A+ RNA using a Stratagene (La Jolla, CA) Lambda ZAP Express kit, following the manufacturer's instructions. Sera was obtained from the colon tumor-bearing SCID mouse. This serum was injected into normal mice to produce anti-colon tumor serum. Approximately 600,000 PFUs were screened from the unamplified library using this antiserum. Using a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (BRL Labs.), positive plaques were identified. Phage was purified and phagemid excised for several clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined cDNA sequences for 46 of the isolated clones are provided in SEQ ID NO: 152-197. The predicted amino acid sequences for the cDNA sequences of SEQ ID NO: 187, 188, 189, 190, 194, 195 and 197 are provided in SEQ ID NO: 198-204, respectively. The determined cDNA sequences were compared with those in the public database as described above. The sequences of SEQ ID NO: 156, 168, 184, 189, 192 and 196 showed some homology to previously isolated ESTs. The sequences of SEQ ID NO: 152-155, 157-167, 169-182, 183, 185-188, 190, 194, 195 and 197 showed some homology to previously identified genes.

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The determined cDNA sequences for an additional eleven clones isolated as described above, are provided in SEQ ID NO: 617-627. Comparison of these sequences with those in the public database as described above revealed no known homologies to SEQ ID NO: 621 and 623. The sequences of SEQ ID NO: 622 and 626 were found to show some homology to previously isolated ESTs, while the sequences of SEQ ID NO: 617-620, 624, 625 and 627 showed some homology to previously identified genes.

In further studies, a cDNA library was prepared from SCID-mouse grown colon tumors and screened with mouse anti-SCID serum as described above. Briefly first strand cDNA was synthesized from poly A+ RNA from three SCID mouse-grown human colon tumors using a Lambda ZAP Express cDNA synthesis kit (Stratagene). The reactions were pooled and digested with RNase A, T1 and H to 30 cleave the RNA and then treated with NaOH to degrade the RNA. The cDNA was annealed with biotinylated cDNA from a normal resting PBMC plasmid library

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(constructed from Superscript plasmid system; Gibco BRL) and subtracted with streptavidin by phenol/chloroform extraction. Second strand cDNA was synthesized from the subtracted first strand cDNA and digested with S1 nuclease. The cDNA was blunted with Pfu polymerase and EcoRI adaptors were ligated to the ends. The cDNA was phosphorylated with T4 polynucleotide kinase, digested with restriction endonuclease XhoI, and size selected with Sephacryl S-400 (Sigma). Fractions were pooled, ligated to Lambda ZAP Express arms (Stratagene) and packaged with Gigapack Gold III extract (Stratagene). The resulting library was screened with a mouse antiserum raised against serum from SCID mice containing human colon tumors, including the three tumors used to prepare the cDNA libraries.

The determined cDNA for one clone isolated using this procedure is provided in SEQ ID NO: 630. This clone was found to show homology to a previously identified gene. The amino acid sequence encoded by the clone of SEQ ID NO: 630 is provided in SEQ ID NO: 631.

In subsequent studies, an additional cDNA library was prepared from a SCID-passaged human colon tumor and screened with a mouse antiserum raised against serum from the SCID mouse containing the colon tumor. The determined cDNA sequences for 51 clones isolated in these studies are provided in SEQ ID NO: 632-682. Comparison of these sequences with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 648 and 668. The sequence of SEQ ID NO: 642 showed some homology to previously isolated ESTs. The sequences of SEQ ID NO: 632-641, 643-647, 649-667 and 669-682 were found to show some homology to previously identified genes. SEQ ID NO: 684 and SEQ ID NO: 690 showed homology to human NADH/NADPH thyroid oxidase p138-tox mRNA.

Example 4

ISOLATION AND CHARACTERIZATION OF COLON TUMOR POLYPEPTIDES BY CONVENTIONAL SUBTRACTION

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Two cDNA libraries were constructed and used to create a subtracted cDNA library as follows.

Using the GibcoBRL Superscript Plasmid System with minor modifications, two cDNA libraries were created. The first library, referred to as CTCL, was prepared from a pool of mRNA samples from three colon adenocarcinoma tissue samples. Two of the samples were described as Duke's stage C and one as Duke's stage B. All three samples were grade III in histological status. A second library (referred to as DriverLibpcDNA3.1+) was prepared from a pool of normal tissues, namely liver, pancreas, skin, bone marrow, resting PBMC, stomach and brain. Both libraries were prepared using the manufacturer's instructions with the following modifications: an EcoRI-NotI 5' cDNA adapter was used instead of the provided reagent; the vector pCDNA3.1(+) (Invitrogen) was substituted for the pSPORT vector; and the ligated DNA molecules were transformed into ElectroMaxDH10B electrocompetent cells. Clones from the libraries were analyzed by restriction digest and sequencing to determine average insert size, quality of the library and complexity of the library. DNA was prepared from each library and digested.

The driver DNA was biotinylated and hybridized with the colon library tester DNA at a ratio of 10:1. After two rounds of hybridizations, streptavidin incubations and extractions, the remaining colon cDNAs were size-selected by column chromatography and cloned into the pCMV-Script vector from Stratagene. Clones from this subtracted library (referred to as CTCL-S1) were characterized as described above for the unsubtracted libraries.

The determined cDNA sequences for 20 clones isolated from the CTCL-S1 library are provided in SEQ ID NO: 462-479, 628 and 629. Comparison of these sequences with those in the public databases, as described above, revealed no significant homologies to the sequences of SEQ ID NO: 476, 477 and 479. The remaining sequences showed some homology to previously identified genes.

In further studies, a cDNA library was prepared from a pool of mRNA from three metastatic colon adenocarcinomas derived from liver tissue samples. All samples were described as Duke's stage D. Conventional subtraction was performed as described above, using the DriverLibpcDNA3.1+ library described above as the

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driver. The resulting subtracted library (referred to as CMCL-S1) was characterized by isolating a set of clones for restriction analysis and sequencing.

The determined cDNA sequences for 7 clones isolated from the CMCL-S1 library are provided in SEQ ID NO: 480-486. Comparison of these sequences with those in the public databases revealed no significant homologies to the sequence of SEQ ID NO: 483. The sequences of SEQ ID NO: 480-482 and 484-486 were found to show some homology to previously identified genes.

Example 5 SYNTHESIS OF POLYPEPTIDES

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Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the trifluoroacetic following cleavage mixture: acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

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CLAIMS

An isolated polypeptide, comprising at least an immunogenic 1. 10 portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

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(a) sequences recited in SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320,

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322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-

441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488,

491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553,

556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648,

668, 682-684, 686, 690-691, and 694-1081;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-

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132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-

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193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and

(c) complements of sequences of (a) or (b).

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- 2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any.of the foregoing polynucleotide sequences.
- 3. An isolated polypeptide comprising a sequence recited in any one of SEO ID NOs: 122 and 198-204.

- An isolated polynucleotide encoding at least 15 amino acid 4. residues of a colon tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID Nos: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any of the foregoing sequences.
- 5. An isolated polynucleotide encoding a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:_ 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-

691, and 694-1081, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081.

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- 7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081 under moderately stringent conditions.
 - 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

- 9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.
- 5 10. A host cell transformed or transfected with an expression vector according to claim 9.
 - 11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a colon tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any of the foregoing polynucleotide sequences.
 - 12. A fusion protein, comprising at least one polypeptide according to claim 1.

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- 13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of

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claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

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- 16. An isolated polynucleotide encoding a fusion protein according to claim 12.
- 17. A pharmaceutical composition, comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:
 - (a) a polypeptide according to claim 1;
 - (b) a polynucleotide according to claim 4;
 - (c) an antibody according to claim 11;
 - (d) a fusion protein according to claim 12; and
 - (e) a polynucleotide according to claim 16.
 - 18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:
 - (a) a polypeptide according to claim 1;
 - (b) a polynucleotide according to claim 4;
 - (c) an antibody according to claim 11;
 - (d) a fusion protein according to claim 12; and
 - (e) a polynucleotide according to claim 16.
- 25 19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.
 - 20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.
 - 21. A method for inhibiting the development of a cancer in a

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patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

- 22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 18.
- 23. A pharmaceutical composition comprising an antigenpresenting cell that expresses a polypeptide according to claim 1, in combination with 10 a pharmaceutically acceptable carrier or excipient.
 - 24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.
- 25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;
 - (b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and
 - (c) complements of sequences of (i) or (ii); in combination with an immunostimulant.
 - 26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.
 - 27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

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- 28. A vaccine according to claim 25, wherein the antigenpresenting cell is a dendritic cell.
- 29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
 - (a) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;
 - (b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and
 - (c) complements of sequences of (i) or (ii)encoded by a polynucleotide recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;

and thereby inhibiting the development of a cancer in the patient.

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- 30. A method according to claim 29, wherein the antigenpresenting cell is a dendritic cell.
- 31. A method according to any one of claims 21, 22 and 29, wherein the cancer is colon cancer.
 - 32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
 - (i) polynucleotides recited in any one of SEQ ID NOs: 1-

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121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

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- 33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.
- 34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.
 - 35. A method for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:
 - (a) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
 - (i) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;
 - (ii) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and

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- (iii) complements of sequences of (i) or (ii);
- (b) polynucleotides encoding a polypeptide of (a); and
- (c) antigen presenting cells that express a polypeptide of (a); under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

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36. An isolated T cell population, comprising T cells prepared

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according

to the method of claim 35.

- 37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.
 - 38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
 - (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
 - (i) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
 - (1) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081
 - (2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and
 - (3) complements of sequences of (1) or (2);
 - (ii) polynucleotides encoding a polypeptide of (i); and
 - (iii) antigen presenting cells that expresses a polypeptide of

(i);

such that T cells proliferate; and

- (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.
- 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
 - (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient

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and

with at least one component selected from the group consisting of:

- (i) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
 - (1) sequences recited in SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081;
 - (2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 under moderately stringent conditions; and
 - (3) complements of sequences of (1) or (2);
 - (ii) polynucleotides encoding a polypeptide of (i); and
 - (iii) antigen presenting cells that express a polypeptide of (i); such that T cells proliferate;
 - (b) cloning at least one proliferated cell to provide cloned T cells;
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.
- 40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 or a complement of any of the foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cutoff value, and therefrom determining the presence or absence of a cancer in the patient.

- 41. A method according to claim 40, wherein the binding agent is an antibody.
- 5 42. A method according to claim 43, wherein the antibody is a monoclonal antibody.
 - 43. A method according to claim 40, wherein the cancer is colon cancer.

- 44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 or a complement of any of the foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of polypeptide that binds to 20 the binding agent;
 - (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in
 the patient.
 - 45. A method according to claim 44, wherein the binding agent is an antibody.
- 30 46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

- 47. A method according to claim 44, wherein the cancer is a colon cancer.
- 48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 or a complement of any of the foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- 15 (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
 - 51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a

polynucleotide sequence recited in any one of SEQ ID NOs: 1-121, 123-197, 205-630 and 632-684, 686, 690-691, and 694-1081 or a complement of any of the foregoing polynucleotide sequences;

- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
 - (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
 - 52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

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53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

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- 54. A diagnostic kit, comprising:
- (a) one or more antibodies according to claim 11; and
- (b) a detection reagent comprising a reporter group.
- 55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.
 - 56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
 - 57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent

groups, enzymes, biotin and dye particles.

- 58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081, or a complement of any of the foregoing polynucleotides.
- 59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648, 668, 682-684, 686, 690-691, and 694-1081.

- 60. A diagnostic kit, comprising:
- (a) an oligonucleotide according to claim 59; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or
- 5 hybridization assay.

1

SEQUENCE LISTING

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 Xu, Jiangchun
 Lodes, Michael J.
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 Benson, Darin R.
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agaataaccc tgatctttac aagttgtggc aataggagaa gatactcaac tcaaatattt atgtttcttc attgtccgaa	tgcggacttg tgaaaaacag	attttgaccc tttgaactgt	gactgcagtt cagaacaaac	ttgtcccaaa	240 300 360 408
<210> 17 <211> 407 <212> DNA <213> Homo sapie	n				
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<210> 18 <211> 405 <212> DNA <213> Homo sapie	n				
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<210> 19 <211> 401 <212> DNA <213> Homo sapie	n				
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<210> 20 <211> 331 <212> DNA <213> Homo sapie:	n				
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331
attectgeca gacceegge tateceggtg g
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      <211> 346
      <212> DNA
      <213> Homo sapien
      <220> .
      <221> misc_feature
     <222> (1)...(346)
     <223> n = A, T, C \text{ or } G
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agateteace agteaegtgg teaattttaa gecaaeetet tgtgteteee eteagtgaat
                                                                       120
agettatgtc cagacettct ggatcettgg cagtcacatt gcccacttta gtgcctatag
                                                                       180
ctacatcctc actgactttc gcttggaata cgtgttggga aaattgaggt gcttcattca
                                                                       240
                                                                       300
catctgtcac aataagncgt gaacttggca aaagaacttg cattgtactt cacaccaaac
actagagget caggatttte tgetttgaac acaatgttgg aaacag
                                                                       346
      <210> 22
      <211> 360
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
     <222> (1)...(360)
      <223> n = A, T, C or G
      <400> 22
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gggactgggc gctaccaggt gcttcttaat gaagaggata actcagaatc atcggctata
                                                                        180
gagcagccac ctacttcaaa cccagcaccc gcagattgtg caggctgcgt cttcagcacc
agcacttgaa actgactctt cccctccacc atatagtagt attactggtg gaagtaccta
                                                                        240
                                                                        300
caacttcaga tacagaagtt tacggtgagt tttatcccgt gccacctccc tatagcgttg
                                                                        360
ctacctctct tcctacnwta cqatqaaaqc tqaqaaqgct aaagctgctg caatggcatg
      <210> 23
      <211> 251
      <212> DNA
      <213> Homo sapien
      <400> 23
                                                                         60
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agaaagtact ccaaccagag atgctgtggt cacgtatact gcagaaagta aaggagtcgt
                                                                        120
gaagtttggc tggatcaagg gtgtattagt acgttgtatg ttaaacattt ggggtgtgat
                                                                        180
                                                                        240
gcttttcatt agattgtcat ggattgtggg tcaagctgga ataggtctat cagtccttgt
                                                                        251
aataatgatg g
      <210> 24
      <211> 421
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(421)
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<222> (1)...(383)

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<223> n = A, T, C or G
      <400> 24
                                                                        60
caggitette ccaggitett actocagete cagetteage tecageteea ggtegggete
                                                                       120
cagetecage egeagettar geageggag gttetgtgte ceagttgttt tecaatttea
                                                                       180
ccggctcccg tggatgamcg ygggacctgy caswgctcct gtktycctgc yagsacacca
cnytttyccg tggacacrar kggaaccket tggaattcac agetyatgtt ettteteara
                                                                       240
                                                                       300
agtttgagaa agaactttct aaagtgaggg aatatgtcca attaattagt gtgtatgaaa
                                                                       360
agaaactgtt aaacctaact gtccgaattg acatcatgga raaaggatac catttcttac
                                                                       420
actgaactgq acttcgagct gatcaaggta gaagtgaagg agatggaaaa actggtcata
                                                                       421
      <210> 25
      <211> 381
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (381)
      <223> n = A, T, C or G
      <400> 25
                                                                        60
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gcaattacaa caatttagga nacaaaacaa tataaacaaa agaatgttaa atagttttt
                                                                       120
ttaaaaaata gcttgttgct tgcaanaaag tccatataat cttattcccc cccaaatata
                                                                       180
                                                                       240
attttatact ttgcactaaa ccaaaatagc ttatggaaaa ttagtattaa atagctaaac
                                                                       300
acagaaaacc tacagctata aataacataa aatacagttt aactttaatg ngatgcttaa
                                                                       360
acaaagcaaa ctatgatgca atatgaatca acttcattaa ttggacaagt ccagnggagg
                                                                       381
cacaaattag ataagcacta a
      <210> 26
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(401)
      <223> n = A, T, C or G
      <400> 26
qqaaaaqqqa ctqqcctctc tqaaqaqtga gatqaqggaa qtggaaqgag agctggaaag
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qaaqqaqctq qaqtttqaca cqaatatqqa tqcaqtacaq atqqtgatta cagaagccca
                                                                       120
                                                                       180
qaaqqttqat accagaaqcc aaqaacqctg qggttacaat ccaagacaca ctcaacacat
tagacgggct cctgcattct gatggaccaa ccttttcang tggtaagatt gaagangggg
                                                                       240
cctqqqctta cctqqqaaqc aaaaactttt cccqanccaa qqaacccaqq attcaaccan
                                                                       300
gcnacttgcn ggccaaggaa ggcanaactn ggaanaaaag gccccttaag caaaagggnc
                                                                       360
                                                                       401
accttcattt gctnggaaan cagcctttan ttggaatctt g
      <210> 27
      <211> 383
      <212> DNA
     <213> Homo sapien
      <220>
      <221> misc_feature
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<223> n = A, T, C or G
      <400> 27
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                                                                        60
gaaaaaatat accacttcat agctaagtct tacagagaan aggatttgct aataaaactt
                                                                       120
aagttttgaa aattaagatg cnqqtanaqc ttctqaacta atqcccacaq ctccaaqqaa
                                                                       180
nacatgtcct atttagttat tcaaatacca gttgagggca ttgtgattaa gcaaacaata
                                                                       240
tatttgttan aactttgntt ttaaattact gntncttgac attacttata aaggagnctc
                                                                       300
taactttcga tttctaaaac tatgtaatac aaaagtatan ntttccccat tttgataaaa
                                                                       360
gggccnanga tactgantag gaa
                                                                       383
      <210> 28
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(401)
      <223> n = A, T, C or G
      <400> 28
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                                                                        60
taacgtggat ggatggacag tttacaatcc agtggaagaa tacaggaggc agggcttgcc
                                                                       120
caatcaccat tggagaataa cttttattaa taagtgctat gagctctgcg acacttaccc
                                                                       180
tgctcttttg gtggttccgt atcgtgcctc anatgatgac ctccggagag ttgcaacttt
                                                                       240
taggtcccga aatcgaattc cagtgctgtc atggattcat ccaqaaaata agacqqtcat
                                                                       300
tgtgcgttgc agtcagcctc ttgtcggtat gagtgggaaa cgaaataaag atgatgagaa
                                                                       360
atatctcgat gttatcaggg agactaataa acaaatttct a
                                                                       401
      <210> 29
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 29
atatgagttt gccatctcca tggatgccat ttcaatgcct tcagggtaat cattctctcc
                                                                        60
ccaaagactg cccacggggt catcactcct gtgacgaaat gagggctgga ttgaagatgt
                                                                       120
tetgetgage accecetgg teatetttgg ggteteagaa gagecataat catgaceatt
                                                                       180
ctcagcatct gaataatcag gttctctcca agtgcttggc aagttctgat tgtcctcagc
                                                                       240
actgggatag tctggctccc caaaaaaggg tggagagtta ggttgaatgt cagcgcctgg
                                                                       300
ataatcaggc tttcccagag agtctgcgta tggattgatt ctaaaacttg tatgttccag
                                                                       360
attctttctg gatcctggat ggttcaaatt ggctctgggt c
                                                                       401
      <210> 30
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 30
cctgaactat ttattaaaaa catgaccact cttggctatt gaagatgctg cctgtatttg
                                                                        60
agagactgcc atacataata tatgacttcc tagggatctg aaatccataa actaagagaa
                                                                       120
actgtgtata gcttacctga acaggaatcc ttactgatat ttatagaaca gttgatttcc
                                                                       180
cccatcccca gtttatggat atgctgcttt aaacttggaa gggggagaca ggaaqtttta
                                                                       240
attgttctga ctaaacttag gagttgagct aggagtgcgt tcatggtttc ttcactaaca
                                                                       300
gaggaattat gctttgcact acgtccctcc aagtgaagac agactgtttt agacagactt
                                                                       360
tttaaaatgg tgccctacca ttgacacatg cagaaattgg t
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<210> 31 <211> 297 <212> DNA <213> Homo sapie	en				
<pre><400> 31 acctccatta atgccaggtg catgccacct ggattgcatc aatgatgcca atgggtggaa aatgccacca ggtatgcccc acaggctgtt tcagcgccag</pre>	atcagagaaa tgatgccacc cacctgttcc	atacacccag tggaccagga acgtcctgga	tcattttgcg ataccacctc attcctccaa	gtgaaaacát tgatgcctgg tgactcaagc	60 120 180 240 297
<210> 32 <211> 401 <212> DNA <213> Homo sapie	en				
<pre><400> 32 caaacctgga gccaaaaagg cagaggttgg ggtgaccaac caagacaagc aacaaaccct agctttaaag aaagtgtttg cctcctcaat ctggtttatg ccccaggatt atgtttgttg attcaaaccg tctctatgct</pre>	tcatctggac tgatgattat ctgaaaataa aaacaactga acccatctct	tcagacatat tcatcacttg agaaatccag caaacacctt gacagttaga	gaagaagete ggtgagtgee aaattggeag teteetgatg geeegatate	tatataaatc cacacagtca agcagtttgt gccagtatgt	60 120 180 240 300 360 401
<210> 33 <211> 401 <212> DNA <213> Homo sapie	∍n				
<pre><400> 33 agcagagga caggaatcat caagcctggc cccagaagat aggccagtga gttggttgtc tgctgaaggc tcagagcttg attataggta ttacttcaaa agatctggga ggatgagacg agcggatcga ttgagccctg</pre>	cacaaagagc acttactttt accctgggcc aaagcaagcg gtgctcccga	caaagaaact tctgtgggga actttaaaga atgagtttgc tgtatgaagg	ggcaggtgtc agaaattcca gcagctcagc ctgtggagcg ccggattctg	cacgcgctcc taccggagga aaaaagggaa gtgtttgagg	60 120 180 240 300 360 401
<210> 34 <211> 401 <212> DNA <213> Homo sapie	en				
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<210> 35 <211> 401 <212> DNA <213> Homo sapie	en				

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<220>
      <221> misc feature
      <222> (1)...(401)
      <223> n = A, T, C or G
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cttcaggtgg tgctccttca ttattccaaq qatqcaqcat ctctatqqtq ccaqqtatqq
                                                                       120
gggtaaagcc tttggcgccc tttccgcaat ggcacatcag cagtaaaagt ggtaccaata
                                                                       180
gcangaacag aaagggcaaa atcatgancg caattgctgc gggtcccaag cccacatagg
                                                                       240
aatcatgctg ngcttccctg canccgctgc catgcaagac actnacaaac tgngantgta
                                                                       300
aggacctgct tttcaggaca actaaaaccc tgattgnctg aaatcaggaa ctgaatttca
                                                                       360
cttctcccaa gctttttctc actttggtgc aacancacac t
                                                                       401
      <210> 36
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 36
cctgctagaa tcactgccgc tgtgctttcg tggaaatgac agttccttgt tttttttgtt
                                                                        60
tctgtttttg ttttacatta gtcattggac cacagccatt caggaactac cccctgcccc
                                                                       120
acaaagaaat gaacagttgt agggagaccc agcagcacct ttcctccaca caccttcatt
                                                                       180
ttgaagttcg ggtttttgtg ttaagttaat ctgtacattc tgtttgccat tgttacttgt
                                                                       240
actatacatc tgtatatagt gtacggcaaa agagtattaa tccactatct ctagtgcttg
                                                                       300
actttaaatc agtacagtac ctgtacctgc acggtcaccc gctccgtgtg tcgccctata
                                                                       360
ttgagggctc aagctttccc ttgttttttg aaaggggttt a
                                                                       401
      <210> 37
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(401)
      <223> n = A, T, C or G
      <400> 37
cnnctntgna atggantnnt tgnctaaaan ganttgatga tgatgaanat ccctangang
                                                                        60
antaagcatg ganentgate ntttnetnng cacteettta egacaeggaa acangnatea
                                                                       120
ncatgatggt accaganacc ttatcaccna cgcgcacnga nctgactnat tccaaagagt
                                                                       180
tgnggttacg gncatccggt cattgctcgt gcccattgct gcagggctga tnctactggt
                                                                       240
gettattatg ntggeeetga ggatgeteea caatgaatat aageatgetg catgateage
                                                                       300
ggcaacanat gctctgccgt ttgcactaca tctttcacgg acacnatntc gaanacgggc
                                                                       360
acnttgcana gttagacttg gaatgcatgg ngccggncan n
                                                                       401
      <210> 38
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 38
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                                                                        60
cagcaaaaaa cagagggga gaaaaaagtc tattattggc ttgtgattta caaaagccaa
                                                                       120
agtcctttag ataaaaggcc aggagtcgta ccaacataga taccaaatcc aggagaacac
                                                                       180
agaccagega taagagggac getteeceat gacccagace agectaaage eeetgtgggg
                                                                       240
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gcagccagtg gggagctgtc agacct tctctccctg accagttggg atagac ctatgaacag agaggactgt gcctgt	acct gactggaato	cttgacactg		300 360 401
<210> 39 <211> 401 <212> DNA <213> Homo sapien				
<220> <221> misc_feature <222> (1)(401) <223> n = A,T,C or G				
<pre><400> 39 tctggtangg agcaattcta ttattt gtgagaacag gtgagtctag aagtcc cggctgtgtt aaagatgctg ctaatg tatgtaaaac gttgggaatg acaaga ctacttcttg tgaaatacta atgaca gcaaggacaa attaaaaggg ggtaag cttgggaaaa gctgtccata gtgtga</pre>	aact ctgaaaagga tcag tcactgggtg tana actgatactc gcat catcctgcca agcc ttatcatgat	ccactgtaca cactaaagga tggtaagtta agcgaaagag gaggagtctt	tttgaacaca tctcttattt ccctctgaag gcaggcataa	60 120 180 240 300 360 401
<210> 40 <211> 401 <212> DNA <213> Homo sapien				
<pre><400> 40 tctggtcacc caactcttgt ggaaga agaggctgga atccttcagc cccaga cctgcccagg ggtcagggca gtgggta aggcatcttt gtttcctggt gccctc gtagaagtag ggctgctcct tttggaa cagtcgggct gtccaggttc taagcaa cagccagagg atcccagcct cctcct</pre>	gccc agggaccact atca ctggtgacat ctca aagttgctga gctg gagggaatag tcac agcttctgca	ccagtagatg caagaatatc cactttgggg acctggagac ctgggctctg	cagagagggg agggctgggg acgggaaggg agagttgagg	60 120 180 240 300 360 401
<210> 41 <211> 401 <212> DNA <213> Homo sapien		·		
<220> <221> misc_feature <222> (1)(401) <223> n = A,T,C or G				
<pre><400> 41 ctggactaaa aatgtccact atggggt aaggggcaga gagtaaaaaa catgacg ggggaggatc aattagagag gaggcac ccatcagcaa aggagcactt ctctaat taaaacaaa aaatccagga gtaagag ctggcaaagg gtgcganagg gagcttg gtangtttct gaagtgtgcc attgggg</pre>	ctgg tagaaggaag cetg ggatecacet ccat geeeteeega geet taggteagtt gtge teangagtee	agaggcaaag tetteettan agaetggetg tgaaattgga ageeegteea	gaaactaggt gtcccctcct ggagaaggtt gacaaactgt	60 120 180 240 300 360 401
<210> 42				

<210> 42 <211> 310

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<212> DNA
      <213> Homo sapien
      <400> 42
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                                                                        60
atacagaaat agcccaaatc tggaaatttt gaattaaaat tgtaatcctg taaaacaagt
                                                                       120
tttqqqqtqa atqqatttct ttaataccaa taatatttt aattcccacc acagatggat
                                                                       180
                                                                       240
ttgctgaata tgctaatgct gtgaatgaga aaacaatttt ggggtaggta tacccacaag
                                                                       300
taatctqatq acaaaataaa ccacagactg atgtcaaatg gacaaaaaac tgaaaatatg
                                                                       310
ctqtqaqaaa
      <210> 43
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 43
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                                                                         60
ctttcatgcc tctgatcatg tgcccaagcc aggagtgcca aaccaaccgc tcaggagggc
                                                                       120
ggctgtatct gcagacacgg ggctccagat tcatcaaatt ccaggagatg aagatgcaag
                                                                       180
aacataqtqa tcaqqtqcct qtqqqaaata tccctcqtaq tatcacqqtq ctqqtagaaq
                                                                        240
                                                                        300
qaqaqaacac aaqqattqcc caqcctggag accacqtcag cqtcactggt attttcttqc
caatcctgcg cactgggttc cgacaggtgg tacagggttt actctcagaa acctacctgg
                                                                        360
                                                                        401
aagcccatcg gattgtgaag atgaacaaga gtgaggatga t
      <210> 44
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 44
                                                                         60
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                                                                        120
ttggcagatt aaatctttgc aaaattccat atgtgctatt gaaaaatgaa ataaaacctc
agatgtctga attcttattt caaatacagt tatataatta ttttaaatta caatatacaa
                                                                        180
tttctgttaa atacaactgt taagggattc tgagaacaat tataagatta taataatata
                                                                        240
                                                                        300
tacaaactaa cttctgaaat gacatgggtt gtttccttcc caccctccta ccctctcaaa
                                                                        360
gagtttttgc atttgctgtt cctggttgca aaaggcaaaa gaaaatctaa aaatagtctg
                                                                        401
tgtgtgtcca cgacatgctc gctcctttga gaatctcaaa c
      <210> 45
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(401)
      \langle 223 \rangle n = A, T, C or G
      <400> 45
                                                                         60
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gctacagtgg gaacaggctc aggactatct caagagattt tatctctatg actcagaaac
                                                                        120
aaaaaatgcc aacagtttag aagccaaact caaggagatg caaaaaattc tttggcctac
                                                                        180
                                                                        240
ctatactgga atggtaaact cccgcgtcat anaaataatg caanaagccc agatgtggag
                                                                        300
tqccagatgt tgcagaatac tcactatttc caaatagccc aaaatggact tccaaagtgg
                                                                        360
tcacctacag gatcgtatca tatactcgag acttaccgca tattacagtg gatcgattag
                                                                        401
tgtcaaaggc tttaaacatg tggggcaaag agatccccct g
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<210> 46
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(401)
      <223> n = A, T, C or G
      <400> 46
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qtcagaattq tctttctgaa aggaaqcact cggaatcctt ccgaactttc caagtccatc
catgattcan agatactgcc ttctctctct ctgggatttt atgtgtttct gatagtgaat
                                                                       120
tgttgatgta tttgctactt tgcttctttt ctctttcaag acttgatcat tttatatgct
                                                                       180
gnttggagaa aaaaagaact tttggtagca aggaggtttc aagaaatgat tttggatttt
                                                                       240
ctgctgcgga atttctcggc acctacctgt agtatggggc acttggtttg gttgcagagt
                                                                       300
aagaaggtgg aagaatgagc tgtacttggt taagcagttg aaaccttttt tgagcaggat
                                                                       360
ctgtaaaagc ataattgaat ttgtttcacc cccgtggatt c
                                                                       401
      <210> 47
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 47
                                                                        60
ggtctgcagc aatgcacttc aaccatacat actgcttcca ctagctaata ccaaatgcag
gttctcagat ccagacaaat ggaggaaaag aacatttatg cttccgtttc agaaagccaa
                                                                       120
gtcgtagttt tggcccttcc tttctctaaa gtttattccc aaaaacaggt agcattcctg
                                                                       180
attgggcaga gaagaggata ttttcagccc acatctgctg caggtatgtc attttctccc
                                                                       240
                                                                       300
atcttcactg tgactagtaa agatctcacc acttctcttt ggaatttcca actttgcttg
tgattgaatg tcacttcgtg aatttgtatt atgtcagatc acttggcatt gctcttccat
                                                                       360
                                                                       401
atgcatcaag ttgccaggca ctaaacccaa tgttcatgaa c
      <210> 48
      <211> 430
      <212> DNA
      <213> Homo sapien
      <400> 48
                                                                        60
acataacttg taaacttttt ctgcttgggg gctgtaacag acagaagagt aaagactaca
                                                                       120
aggattttct gaaqatqctt caatqaaaat catcatttcc tctttagtca tcccaagtct
tggtttgaaa aacttgggca tggacttata cagaccttga accaccactg acttatcatt
                                                                       180
gggtggcaga ccttgaaacc aagctctctg tgttacttct gaaagtgcat caattctgat
                                                                       240
ttggctaaga acagaagaca aatactggga tcgtgattct gtgttatact ctagccacag
                                                                       300
catagoaget tetegaacgg tttetteett ttetacattt aaattgteac tactgagaat
                                                                       360
atctatcagt aggtcatgtg acagacctgc cccggggccg gcccgctcga tgcttgccga
                                                                       420
atatcatggt ·
                                                                       430
      <210> 49
      <211> 57
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc_feature
    <222> (1)...(57)
     <223> n = A, T, C or G
```

```
<400> 49
ggtattaaca atatcangca ctcattcttc ccctcttatg aaanggatna attttta
                                                                         57
      <210> 50
      <211> 327
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(327)
      <223> n = A, T, C \text{ or } G
      <400> 50
gatggnggtn tccacaagan tnaangtncn tattaantan nncttgtaga nccacttnna
                                                                         60
ttaattgnnn tatgnntgnc cttctggtgg ntgtngaagc ttcatatnnt ntttggacat
                                                                        120
cattacacgt cttagctctt tnaagnacaa ctttaatgct atatgaattt tgccattttn
                                                                        180
gctaacactg gtatgctccn ngcatccacc atnccacntg gaattattta ttncnttcat
                                                                        240
attaatnttt tgtttaccaa atctnacttg acccgaacga aactttctgn gtattttang
                                                                        300
gccccnccat tcttactttt caagcct
                                                                        327
      <210> 51
      <211> 236
      <212> DNA
      <213> Homo sapien
      <400>.51
cgtctcgaag aagcgctgca ggccgatgat ggactgcacg tctgccttgt cctcagttaa
                                                                         60
cttgttgaat tgcttgaaca tgcggcccac atcctgggca aactcctgtg gggagctgta
                                                                        120
gggaggtgac aacttctcct ggaggcgggc acggatcagg gtcagatcca gggtgccacc
                                                                        180
gggctggtcc agggagaagg tggagtcgta gccagacctg cccgggcggc cgctcg
                                                                        236
      <210> 52
      <211> 291
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(291)
      <223> n = A, T, C or G
      <400> 52
ctcacatcct gggtccggct gtagagctgc accatggtgc tgagcgcccc ctccagctcc
                                                                         60
ttgtagatgt aaaggacggc gaaggagctg tagtctgtgt ccacgatgcg cacgtccagg
                                                                        120
tagcccaagg ccgggactct gaagttgtcc ctcggagccc accttcangt actcgggcat
                                                                        180
ccacctggtt acagcentte gneeteggna actecatntg gaetttacag geegeetee
                                                                        240
tctgtgggcc tgatggncct tgcaggacat nggaacacgg gagctcnctt t
                                                                        291
      <210> 53
      <211> 95
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(95)
      <223> n = A, T, C \text{ or } G
```

```
<400> 53
                                                                         60
gtctgtgcag tttctgacac ttgttgttga acatggntaa atacaatggg tatcgctgan
                                                                         95
cactaagttg tanaanttaa caaatgtgct gnttg
      <210> 54
      <211> 66
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(66)
      <223> n = A, T, C or G
      <400> 54
                                                                         60
cctnaatnat ntnaatggta tcaatnnccc tgaangangg gancggngga agccggnttt
gtccgg
                                                                         66
      <210> 55
      <211> 265
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(265)
      <223> n = A, T, C or G
      <400> 55
                                                                         60
atctttcttc tcagtgcctt ggccntgttg agtctatctg gtaacactgg agctgactcc
ctgggaagag aggccaaatg ttacaatgaa cttaatggat gcaccaagat atatgaccet
                                                                        120
gtctgtggga ctgatggaaa tacttatccc aatgaatgcc gtgttatgtt tttgaaaatc
                                                                        180
ggaaacgcca gacttctatc ctcattcaaa aatctgggcc ttnctgaaaa ccagggtttt
                                                                        240
                                                                        265
naaaatccca ttcnggtcnc cggcg
      <210> 56
      <211> 420
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(420)
      <223> n = A, T, C or G
      <400> 56
gagcggccgc ccgggcaggt cctcgcggtg acctgatggg atttcaaaac cttggttctc
                                                                         60
agcaaggccc agatttttga atgangatag aagtctggcg tttccgattt tcaaaacata
                                                                        120
acacgcattc attgggataa gtatttccat cagtcccaca gacngggtca tatatcttgg
                                                                        180
gtgcatccat taagttcntt tgttaacatt tgggcctctc tttcccangg gaattcagct
                                                                        240
cccagttgtt taccaanatt naactccacc ggggccaaag gcncttgaaa aaaaaaanaa
                                                                        300
ttccttgttt accttccttg ggcttnaagt tctggcgtcc aaaagttcaa tttgaaaact
                                                                        360.
qcaccgcact taccacgtct cttcnagaan cctggggaca cctcggccgc gaccacgcta
                                                                        420
     <210> 57
      <211> 170
      <212> DNA
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<213> Homo sapien <400> 57 60 gaagcggagt tgcagcgcct ggtggccgcc gagcagcaga aggcgcagtt tactgcacag gtgcatcact tcatggagtt atgttgggat aaatgtgtgg agaagccagg gaatcgccta 120 170 gactetegea etgaaaattg teteteeaga eeteggeege gaceaegeta <210> 58 <211> 193 <212> DNA <213> Homo sapien <400> 58 attttcagtg cgagagtcta ggcgattccc tggcttctcc acacatttat cccaacataa 60 ctccatgaag tgatgcacct gtgcagtaaa ctgcgccttc tgctgctcgg cggccaccag 120 180 gegetgeaac teegetteat eggettegee eageteegee attgttegee acetgeeegg 193 qcqqccqctc gaa <210> 59 <211> 229 <212> DNA <213> Homo sapien <400> 59 cgcaactctc gagcatttat atacaatagc aaatcatcca gtgtgttgta cagtctataa 60 tactccaaca gtctcccatc tgtattcaat ggcgccaccc aatacagtcc tttgtttgga 120 180 tgctggggag agtaatccct acccaagca ccatatagat aagaaaaccc tctccagttg 229 agctgaacca cagacggttt gctgatacct gcccgggcgg ccgctcgaa <210> 60 <211> 340 <212> DNA <213> Homo sapien <400> 60 60 tegageggee geeegggeag gteetetaaa gateaaaaca eeeetgtegt eeaceeteet cccactccag ggaagctgtg gtcatggtgg tgtggtgaac atcagcaaac cgtctgtggt 120 180 tcagctcaac tggagagggt tttcttatct atatggtgct tggggtaggg attactctcc 240 ccagcatcca aacaaaggac tgtattgggt ggcgccattg aatacagatg ggaaactgtt 300 ggagtattat aaactggtac aacactgg atgatttgct attgtatata aatgctcgag 340 aattgcggat cacctatgga cctcggccgc gaccacgctg <210> 61 <211> 179 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(179) <223> n = A, T, C or G<400> 61 tttttgtgac ggacgnttgg agtacatgtc ccaggatcac atccagcagc tagagtggct 60 gggacaaget ggeggnggee aageaetgtt gaaacnatag gggtetgggn gnaetegggt 120 tnaagtggtt ggtccgantn ttnataacct tgtcngaacc nancatctcg gttgncang 179

```
<211> 78
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(78)
     <223> n = A, T, C \text{ or } G
     <400> 62
                                                                     60
agggcgttcg taacgggaat gccgaagcgt gggaaaaagg gagcggtggc nggaagacgg
                                                                     78
ggatgagctt angacaga
     <210> 63
     <211> 410
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(410)
     <223> n = A, T, C or G
     <400> 63
cccagttact tggggaggct gaggcaggga gaatcetttg aacccggngg gtgggaggtt
                                                                     60
gcagtgagcc cgagatagca ccattgcact tccancatgg ggtggacaga gtgagactct
                                                                    120
180
tntcccattt caagtcctga aaatagagga tcagaaatgt tgaggaattc tttaggatag
                                                                    240
aaagggagat gggattttac ttatggggaa agaccgcaaa taaagactgn aacttaacca
                                                                    300
cattccccaa gtgnaaggtg ttacccaaga agtaggaacc cttttggctn ttaccttacc
                                                                    360
                                                                    410
ttccngaaaa aaacttattn cttaaaatgg aaacccttaa agcccgggca
     <210> 64
     <211> 199
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(199)
     <223> n = A, T, C or G
     <400> 64
cttgttctca aaaaggtcaa agggagcccg acgaggaata aatagcaatg ccctgaattc
                                                                     60
caactgacct tctacagaaa agtgcttgac tgccaagtgg tcttcccagt cattagtgag
                                                                    120
getettgtag aatteteeat acteetettg ggngangnea tnagggtttn nggeecaaat
                                                                    180
                                                                    199
aggntgggcc tngttaagt
     <210> 65
     <211> 125
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(125)
     <223> n = A, T, C or G
```

<210> 70

```
<400> 65
                                                                        60
ageggtacag ttctgtcctg gcatcatcat tcattgtagt atggtcaata ggtgccatga
                                                                       120
aactcagtag cttgctaagg acatgaaacc gaagtttcct gcctttgctg gcctngtngn
                                                                       125
gggta
      <210> 66
      <211> 204
      <212> DNA
      <213> Homo sapien
      <400> 66
                                                                        60
attcagaatt ctggcatcgg tatttctata aagtccatca gttagagcag gagcaggccc
ggagggacgc cctgaagcag cgggcggaac agagcatete tgaagagccc ggctgggagg
                                                                        120
aggaggaaga ggagctcatg ggcatttcac ccatatctcc aaaagaggca aaggttcctg
                                                                        180
                                                                        204
tggacctcgg ccgcgaccac gcta
      <210> 67
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(383)
      <223> n = A, T, C \text{ or } G
      <400> 67
                                                                         60
teagggeete caggeageca gttttgeagg anatteagea cetagngtet teetgeetna
                                                                        120
cgctcccaag aacctgctcc tgcaggggga acatcagaac tcgtccttga tgtcaaaatg
gggctggtct tnaggcttga agtccaggtt agggctgcca tcctcattga gaattctccg
                                                                        180
ggcagtgtan ccgacgatgg ggtatttggc tttgtacact ttggtgaaaa cctnatccag
                                                                        240
                                                                        300
ggcctccagt tccttggccg tganacccgt antgtcatgg gtgaggtctg caggatccaa
ggacatcttg gctacccctc tagtggagtc cttccccgtc aaggcattgt aaggggctcc
                                                                        360
                                                                        383
tcgtccataa aactcctttt cgg
      <210> 68
      <211> 99
      <212> DNA
      <213> Homo sapien
      <400> 68
tcacatctcc ttttttttt aactttttca aatttttgtg ttaaatagaa ggctaaaggg
                                                                         60
                                                                         99
ttagatttaa gtttctgcta cattgaccct atttaccta
      <210> 69
      <211> 37
       <212> DNA
      <213> Homo sapien
      <220>
       <221> misc feature
       <222> (1)...(37)
       <223> n = A, T, C or G
       <400> 69
                                                                         37
gagaaggacn tacggncctg ntantanang aatctcc
```

```
<211> 222
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(222)
      <223> n = A, T, C or G
      <400> 70
qtqqqtcatt tttqctqtca ccaqcaacqt tqccacqacq aacatccttg acagacacat
                                                                         60
                                                                        120
tettgacatt gaageceaca ttgteeceag gaagagette aeteaaaget teatggegea
tttcgacaga ttttacttcc gttgtaacgt tgactggagc aaaggtgacc accataccgg
                                                                        180
                                                                        222
gtttgagaac acccantcac ctgccccggg cggccgctcg aa
      <210> 71
      <211> 428
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (428)
      <223> n = A, T, C or G
      <400> 71
caggagtatt ttgtagaaaa gccagaagag cattagtaga tgtatggaaa tatacggtag
                                                                         60
                                                                        120
ggcacacgct gacagtactt ttcccaagcc acgccgtatt tcttcttaca gtggtactcg
                                                                        180
tcacqaqctt ctcqqtqqac aaqcaacatq qtqaaataaa ttatqtaqaa ataaqqcaqa
                                                                        240
atqtqqttaa aaccacatqq qaqqqaccac qccaagqcca tgatqagatc acccaagtaa
ttqqqqtqgc qaacaaagcc ccaccatcca gaaactagaa naatttttcc cgttgaaata
                                                                        300
                                                                        360
tqaatqqntt ttaaatqtqc aaqctttqqa tcactgqqaa ttttcccqaa tqcctttttc
                                                                        420
tganaattgc accttnggaa gantccttac cccaagnttc agaccattat ttnaaaagcn
                                                                        428
ttggaact
      <210> 72
      <211> 264
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(264)
      <223> n = A, T, C or G
      <400> 72
                                                                         60
gaataaagag cttactggaa tccagcaggg ttttctgccc aaggatttgc aagctgaagc
                                                                        120
tctctqcaaa cttgatagga gagtaaaaag ccacaataga gcagtttatg aagatcttgg
aggagattga cacacttgat cctgccagaa aatttcaaag acagtagatt gaaaaggaaa
                                                                        180
                                                                        240
qqctttqqta aaaaaaggtt caggcattcc tagccgantg tgacacagtg gagcanaaca
                                                                        264
tetgeangag actganegge tgea
      <210> 73
      <211> 442
      <212> DNA
      <213> Homo sapien
     <220>
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```
<221> misc feature
      <222> (1)...(442)
      <223> n = A, T, C or G
      <400> 73
ggcgaatccg gcgggtatca gagccatcag aaccgccacc atgacggtgg gcaagagcag
                                                                        60
                                                                       120
caagatgctg cagcatattg attacaggat gaggtgcatc ctgcaggacg gccggatctt
                                                                       180
cattggcacc ttcaaggctt ttgacaagca catgaatttg atcctctgtg actgtgatga
                                                                       240
gttcagaaag atcaagccaa agaacttcaa acaagcagaa agggaagaga agcgagtcct
cggtctggng ctgctgccaa gggagaatct ggtctcaatg acngtagaag gaccttcttc
                                                                       300
                                                                       360
caaagatact ggnattgctc gagttccact tgctggaact tcccggggcc caaggatcgc
                                                                       420
aaggettetg geaaaagaaa teeanaettn ggeegggaee aeetaaneea atteacaeae
                                                                       442
tggcggccgt actagtggat cc
      <210> 74
      <211> 337
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(337)
      <223> n = A, T, C or G
      <400> 74
                                                                        60
ggtagcagcg tctccagagc ctgatctggg gtcccagata cccaggcagc agcagccctg
gaggtaaagg gcaagctccc caatgtgagg ggagacccca ttcctggtca gccaggcttt
                                                                       120
cagaggagat agcaggtcga gggagccaac gaagaagaga ctgccancag gggaaggact
                                                                       180
                                                                       240
qtcccqccaa qqacaqaact qattcaqqqq qqtcaatqct cctctagaga agagccacac
                                                                       300
agaactgggg ggtccaggaa ccatgaanct tggctgtggt ctaaggagcc aggaatctgg
                                                                       337
acagtqttct gggtcatacc aggattctgg aattgta
      <210> 75
      <211> 588
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(588)
      <223> n = A, T, C or G
      <400> 75
                                                                        60
catgatgagt totgagotac ggaggaacco toatttooto aaaagtaatt tatttttaca
                                                                        1.20
gcttctggtt tcacatgaaa ttgtttgcgc tactgagact gttactacaa actttttaag
acatgaaaag gcgtaatgaa aaccatcccg tccccattcc tcctctctc tgagggactg
                                                                       180
gagggaagcc gtgcttctga ggaacaactc taattagtac acttgtgttt gtagatttac
                                                                        240
                                                                        300
actttgtatt atgtattaac atggcgtgtt tatttttgta tttttctctg gttgggagta
                                                                       360
tgatatgaag gatcaagatc ctcaactcac acatgtagac aaacattagc tctttactct
ttctcaaccc cttttatgat tttaataatt ctcacttaac taattttgta agcctgagat
                                                                        420
caataagaaa tgttcaggag agangaaaga aaaaaaatat atgttcccca tttatattta
                                                                        480
                                                                        540
gagagagacc cttantcttg cctgcaaaaa gtccaccttt catagtagta ngggccacat
                                                                        588
attacattca gttgctatag gncagcactg aactgcatta cctgggca
      <210> 76
      <211> 196
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<212> DNA <213> Homo sapien WO 01/49716 PCT/US00/35596

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<400> 76
                                                                        60
gcggtatcac agcctggccc ccatgtacta tcggggggcc caggctgcca tcgtggtcta
tgacatcacc aacacagata catttgcacg ggccaagaac tgggtgaagg agctacagag
                                                                       120
                                                                       180
graggerage cecaacateg teattquart egegggtaac aaggeagace tggacetgee
                                                                       196
cgggcggccg ctcgaa
      <210> 77
      <211> 458
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(458)
      <223> n = A, T, C or G
      <400> 77
                                                                        60
agtagagatg gggtttcact gtgttaacca ggatggtctt gatctcctgg cctcgtgatc
                                                                       120
tgcccgcctc ggcctcccaa agtgttggga ttacaggcgt gaaccaccgc acccggccag
aaatgttagt ttttccctat tctctctct ttttcctatt atatacttgg tcaaccagac
                                                                       180
agccatccta ccccanaatg gtaatgcctc ttcattcctc atatgaggga ataaaagaga
                                                                       240
                                                                       300
aaaaagettt tggaaaacat ccacttatct aatcatccca aatatgtaat caaaagtata
caactcatgt gaagaataca ctggtaaaat gttantatag gccaaggtat cttgaattcc
                                                                       360
tatatagaaa gctggtaaat gcccttttgg ctggaaccgc catcttccnn taattcnccc
                                                                       420
                                                                       458
aaaatgacca aacacaaagg gnaagangan aagccccc
      <210> 78
      <211> 464
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(464)
      <223> n = A, T, C or G
      <400> 78
                                                                        60
teegeaaatt teetgeegge aaggteeeag catttgaggg tgatgatgga ttetgtgtgt
ttgagagcaa cqccattgcc tactatgtga gcaatgagga gctgcgggga agtactccag
                                                                       120
aggcagcagc ccaggtggtg cagtgggtga gctttgctga ttccgatata gtgcccccag
                                                                       180
ccaqtacctg ggtgttcccc accttgggca tcatgcacca caacaaacag gccactgaga
                                                                       240
                                                                       300
atgcaaagga ggaagtgagg cgaattctgg ggctgctgga tgcttacttg aagacgagga
cttttctggt gggcgaacga gtgacattgg ctgacatcac agttgtctgc accctgttgt
                                                                       360
ggctctataa gcaggntcta gaaccttctt ttcgcangac cttcggccgg accacgctta
                                                                       420
acccaaattc cacacattg enggeegtac taanggaatc ccac
                                                                       464
      <210> 79
      <211> 380
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(380)
      <223> n = A, T, C or G
      <400> 79
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```
ctgtatgacc agtttttcca tctccttcac ttctaccttg atcagctcga agtccagttc
                                                                        60
agtgtaagaa atggtatcct tctccatgat gtcaattcgg acagttaggt ttaacagttt
                                                                       120
cttttcatac acactaatta attggacata ttccctcact ttanaaagtt ctttctcaaa
                                                                       180
cttctganaa aagaacatga actgtgaatt ccaagcgttc ccactctgtc cacgggaaaa
                                                                       240
ggtggtgtct ggcagggaaa cagaacactg gcaggtccac ggtcatccac ggagccggtg
                                                                       300
aaattgggaa aacaactggg acacagaacc tccgctgcct aagctgcggn tgggagcttg
                                                                       360
                                                                       380
qaacccgacc tggaactgga
      <210> 80
      <211> 360
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(360)
      <223> n = A, T, C or G
      <400> 80
tegageggee geeegggeag gteeteagag agetgtttgt tnegettett caaaaactee
                                                                         60
                                                                        120
tattctccac ttctgctaaa ggactggatg acatcaattg tgatagcaat atttgtgggt
gttctgtcan ncancatcgc actcctgaac aaagtagatg ttggattgga tcagtctctt
                                                                        180
tccacccaga tgactcctan atggtggatn atttcaaatc catcantcag tacctgcatg
                                                                        240
cgnggtccgc ctgtgtnctt tgtcctgcag gangggcnct actacacttc ttccnagggg
                                                                        300
canaacatgg tgtgcngcgg ccatgggctg gcaacantga ttcnctgctg cacccanatn
                                                                        360
      <210> 81
      <211> 440
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(440)
      <223> n = A, T, C \text{ or } G
      <400> 81
acgtggtccg gcgagtctga cctgcagata tgaactcctt gggaaaccta cattctgcct
                                                                         60
cagacatact gggggcaaat ggctttaaaa gtctggctca gggagccaag attacagaaa
                                                                        120
nccgttgagt cnccatacat ggacactgac aaaggaactg aagatatcca aacaagccct
                                                                        180
cctggtcccg ngcctgcata aagatcggga ncggaacggt accngacgtc tgtggtcagg
                                                                        240
ggttgtggaa aattggaaaa aaccagtcct gcccacattg acagggaagc ctcaacggaa
                                                                        300
attgaacaga tngtcttatc accagtctcc cctcctggat cntgtctcgg ctcnggggan
                                                                        360
tcagtgatca gtcctttcag gtggaagaag caaagaagat caacaanaag cngatcctct
                                                                        420
                                                                        440
cacctgntac cagcatatgg
      <210> 82
      <211> 264
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
       <222> (1)...(264)
      <223> n = A, T, C or G
       <400> 82
```

agegtggteg eggeegangt cetgacatte etgeettett atattaatta tacnaataaa

```
acaaaatagt gttgaagtgt tģgagcggcg aaaatttttg gggggtggta tggacagaga
                                                                       120
atgggcgatn ttctcanggc tgcttcaagt gggattgggg cngcgtggga tcatncagtg
                                                                       180
                                                                       240
gganagattn cnctgaccgg antctnttgg tanggatnat cttgtgggga tgtgcaagag
ncattcgtct cctgaatgan tggt
                                                                       264
      <210> 83
      <211> 410
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(410)
      <223> n = A, T, C or G
      <400> 83
ancettagtes eggeegangt ceacagttst sagagaseea secattsts gagagetee
                                                                        60
acaggtaaga ctcgtgtcct gagcagcgca catcatccag gacaatgggt cctgagccct
                                                                       120
gaccaaaccg ggcatttcct ggggctgaca tggcccagcc acagcccant tgcctgcaga
                                                                       180
                                                                       240
cgaaattggc atcattggtg teccagtant catcacaca ggtgccccag gaacctccgg
tatangaact ccactoggcc tonanacctg togcctocat tocncagoot cagggggcaa
                                                                       300
actgggattc agatcettct gtgggtacag gtggtgatat cctgacaggc caactttctg
                                                                       360
gcctgagtgt tgactgangc tgggcagacc tgcccgggcg gccgctcgaa
                                                                       410
      <210> 84
      <211> 320
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(320)
      <223> n = A, T, C or G
      <400> 84
                                                                        60
tegaacggee geeegggeag gtetgeecea ggtgtateea tttgeegeeg atetetatea
naaggagetg getaccetge nnegacgaan teetgaanat aateteacce neecagatet
                                                                       120
ctctgtcgca atggagatgt cgtcatcggt ggncctgatc acagggcatt ggactcagag
                                                                       180
anangtnanc acagtgtnga agcgattgan nnagttcagt tgctggtctt acccgatntt
                                                                       240
ggaaggaagg aaaacgtgtt angacgtatc tcgatgnant tgaccaaanc tgaangctnc
                                                                       300
agggggcatc gcaaaganan
                                                                       320
      <210> 85
      <211> 218
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(218)
      <223> n = A, T, C or G
      <400> 85
tegageggee geeegggeag gtetgetgee egtgetggtg ceattgeece atgtgaagte
                                                                        60
actgtgccag cccagaacac tggtctcggg cccgagaaga ctcctttctc caggctntan
                                                                       120
gtatcaccac taaaatctcc aggggcacca tnganatcct gggtgtccgc aatgttgcca
                                                                       180
atgtctgtcc gcnnattggc tacccaactg ttgcatca
                                                                       218
```

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```
<210> 86
      <211> 283
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (283)
      <223> n = A, T, C or G
      <400> 86
tcgacttctt gtgaaggttt tgganaaata tgtatcagtt cgttttattt gggtattcaa
                                                                         60
taatateett ggtgataatg etgaeteeat ggettetgae eecaaaaatt gaeeetgetg
                                                                        120
ccactggttg tagccctgag attgattttt gtagccacga ttgtttcctc gtcctctgaa
                                                                        180
                                                                        240
gtnctggttg tanttccctc tgtngggcat tcccctctgt tgtanttccc tctgtttgan
                                                                        283
taactaccac ggccaggaaa aacaggggca cgaaggtatg gat
      <210> 87
      <211> 179
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(179)
      <223> n = A, T, C or G
      <400> 87
                                                                         60
agcgtggtcc cggccgatgt ctttctgtgt aagtgcataa cactccacat acttgacatc
cttcangtca cgggccagct nttcagcant ctctggagtg ataggctact gtntgttctn
                                                                        120
ggcaagtgtc tcaanaatac aggggtcntc tctgagatga ntttcagtcc cgaaccctc
                                                                        179
      <210> 88
      <211> 512
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(512)
      <223> n = A, T, C \text{ or } G
      <400> 88
tcgagcggcc gcccgggcag gtcctancan agaatcacca aatttatgga gagttaacag
                                                                         60
gggtttaaca ggaangaagt gcctttagta agttctcaag ccagangctg gaggcagcag
                                                                        120
ctaaatcaga ggacaggatc ctcagtgaaa gtgagccatt cggggtggca tgtcactcca
                                                                        180
ggaataagca caacttanaa acaaatgatt tcgtangata gcacagtgac attggtgcac
                                                                        240
ttgtgaacct gaggccactg tgtcaaactg tgcactggtt gtgaataggg aganccaaaa
                                                                        300
attatgtcct actgggtaat gagetttcaa tgggetegat ceteteacne tgaaagetet
                                                                        360
qtaqaqcaqc tcagaaccac aaccactccc aacattqacc cttctqqqqq tactqtctqt
                                                                        420
qqcacccaca gqaaqqaqct qqaqatcccc attaqqactq tccacccaca cttgaaqcca
                                                                        480
                                                                        512
caaaactgca cctcggccgc gaccaccgct ta
      <210> 89
      <211> 358
      <212> DNA
      <213> Homo sapien
```

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<220>
      <221> misc feature
      <222> (1)...(358)
      \langle 223 \rangle n = A, T, C or G
      <400> 89
                                                                          60
tegageggge egecegggea ggtetgeeag tececatece agacattett tgeatetaag
ctgangtctg aactgagtgg ggtgggctgg tgtttccatc ctcacaactc cagtgagccg
                                                                         120
ggtgtggccg tggcctgcgt ctctctggcg gttagtgatg ttggcatcat ccaccttttt
                                                                         180
caaaacaaaa gcactggact gaagaanaat cccnccctgt ntccacccag tccatggttt
                                                                         240
ttaataaaag ggttatnnaa gttgancaag ncatcaccac acacaancct aagaacnttt
                                                                         300
ttcatcnntc cccaaaacaa accencacce tgggaactee gggegegaac cacgeeta
                                                                         358
      <210> 90
      <211> 250
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(250)
      \langle 223 \rangle n = A, T, C or G
      <400> 90
                                                                          60
cgagcggccg cccgggcagg tctggatggg gagacggact ggaactgcgg cttcccgtgg
cctgcacgca caaggctccc cacggccgcc gaccttcttc agattcgatc gtatgtgtac
                                                                         120
gcacnaagag ccaaatattg acattcacaa cttcgtggga atnttacccc anaagactgc
                                                                         180
                                                                         240
gaccccccga tcaggcgana gcctgagcat agaagaacac cgctgtgggc ttggcactgt
gggncccatc
                                                                         250
      <210> 91
      <211> 133
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (133)
      <223> n = A, T, C or G
      <400> 91
                                                                          60
tcgagcggcc gnccgggcag gtcccgggtg gttgtttgcc gaaatgggca agttcntnaa
                                                                         120
ncctgggaag gtggtgcntg tnctggctgg acgctactcc ggacgcnaag ctgtcntcgt
gangancatt gat .
                                                                         133
      <210> 92
      <211> 232
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(232)
     <223> n = A, T, C or G
      <400> 92
agcqtqqtcg cqgccgangt ctgtcacttt gcqqqqqtag cggtcaattc cagccaccag
                                                                          60
```

agcatggctg taggggggat ctgaggtgcc atcatcaatg ttcttcacga tgacaagctt

```
tgcgtccgga gtagcgtcca gccaggacaa gcaccacctt cccacgtntt cangaactng
                                                                       180
                                                                       232
cccatttcgg cataaccacc cgggacctgc ccgggcggnc gctcgaaaag cc
      <210> 93
      <211> 480
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(480)
      <223> n = A, T, C or G
      <400> 93
agcgtgggtc gcggccgang tctgtangct caccggccag agaagaccac tgtgagcatt
                                                                        60
ttgccgtata tcctgccctg ccatttgttc actttttaaa ctaaaatagg aacatccgac
                                                                       120
                                                                       180
acacaccgtt tgcatcgtct tctcccttga tattttaagc attttcccat gtcgtgagtt
                                                                       240
tctcagaaac atgtttttaa caattgtact atttagtcat ngtccattta ctataattta
tctgaccatt tccctactgt taaaatactt aagacggttt ctgatttttc cactatttaa
                                                                       300
                                                                       360
ataatgctqt qatqaatatc tttaaaatct tctqatttct tacttttttc ccccttagat
gcctggaagt ggtattttga ggtgaaagag tttgttcatt ttgaanatat ttctgtctct
                                                                       420
                                                                        480
ctctcqacct qatqtqtana cqctcacttc caqttagcag aaccacctta gtttgtgtct
      <210> 94
      <211> 472
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(472)
      <223> n = A, T, C or G
      <400> 94
                                                                         60
tcgagcggnc gcccgggcag ggtctgatgt cantcacaac ttgaagggat gccaatgatg
taccaatcon atgtgaaatc totoototta totootatgo tgganaaggg attacaaagt
                                                                        120
tatgtggcng ataannaatt ccatgcacct ctantcatcg atgagaatgg agttcatgan
                                                                        180
                                                                        240
ctggtgaacn atggtatctg aacccgatac cangttttgt ttgccacgat angantagct
                                                                        300
tttattttttg atagaccaac tgtgaaccta ccacacgtct tggacnactg anntctaact
atconcaggg ttttattttg cttgttgaac tcttncagct nttgcaaact tcccaagatc
                                                                        360
                                                                        420
canatgactg antitcagat agcattitta tgattcccan ctcattgaag gtcttatnta
                                                                        472
tntcnttttt tccaagccaa ggagaccatt ggacctcggc cgcgaccacc tn
      <210> 95
      <211> 309
      <212> DNA
      <213> Homo sapien
     <220>
      <221> misc feature
      <222> (1)...(309)
      <223> n = A, T, C \text{ or } G
      <400> 95
togagoggco gcccgggcag agtgtcgago cagogtcgcc gcgatggtgt tgttggagag
                                                                         60
cgagcagttc ctgacggaac tgaccagact tttccanaag tgccggacgt cgggcancgt
                                                                        120
ctatatcacc ttgaagaant atgacggtcg aaccaaaccc attccaaaga aangtactgt
                                                                        180
gganggettt ganceegeag acaacnagtg tetgttaaga actaeegatn ggaaanaana
                                                                        240
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```
anatcagcac tgtgggtgag ctccnaggga agttaataan tttcggatgg gcttattcna
                                                                        300
acctcctta
                                                                        309
      <210> 96
      <211> 371
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(371)
      <223> n = A, T, C or G
      <400> 96
togagoggco gecogggcag gtocaccact cacctactec cogtotetat agatttgcet
                                                                         60
gttctgggca gttctcagca atggaatcct actgtgtatc tttttgtgac tggttcttta
                                                                        120
actcagcatc acattitcaa ggttcatcca tgctgcagcc tggctccgta ctggtgacag
                                                                        180
tacttcattt ctctctccct tttgttcaga ccaaggtctc cctctgtccc caaggctaaa
                                                                        240
gtgcagttgg tgtgatcatg gctcactgca gcctcaaact cctggactca aacagtcctc
                                                                        300
ccatctcagc ctcccaaaqt qctqatntta taaqttqcaa qccctqcacc caqcctqtat
                                                                        360
                                                                        371
ctccagtttg t
     . <210> 97
      <211> 430
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(430)
      <223> n = A, T, C or G
      <400> 97
tcgancggcc gcccgggcag gtttnttttn tttnttttt nnnngntagt atttaaagan
                                                                         60
atttattaaa tcatcttatc accaaaatgg aaacatnttc caactagaaa catgcnacca
                                                                       120
                                                                       180
tcatcttccc cagtccagtc ncaangtcca atattttnct tgcctctgca gataaaaagt
tennattttt atacceacte ttacteccee ecaaaatttt aattengtee tneectaaaa
                                                                       240
                                                                       300
ttncnccggg taacaantta ccaaaatggc naaccaatta ttttaaanaa aagttgcncn
ttnaaaangg aaactttntg gcaanttanc ctcttttccc ttcccacccc ccantttaag
                                                                       360
gggaaaacaa tggcactttg ctcttgcttn aacccaaaat tgtcttccaa aaactattaa
                                                                       420
aaatgttnaa
                                                                       430
      <210> 98
      <211> 307
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(307)
      <223> n = A,T,C or G
      <400> 98
tenaacggce geeenggenn gtetngenge acetgtgeet cancegtega tacetggteg
                                                                        60
attgggacan ggaanacaat ntggttttca gggaggccac anatttggag aaacggatga
                                                                       120
atteteettt atteegaant eageteettg gteteegtag anggtgatet tgaaattete
                                                                       180
ctqttttgaa aactttcttg aanaaacctt acctqctqqt tqtatttggt ctcccactcg
                                                                       240
qacaaqtact cqttatccnn ggtactctta atqtqcccac qtnaactccc cqqqntggca
                                                                       300
```

```
307
actggaa
     <210> 99
     <211> 207
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(207)
      <223> n = A, T, C or G
      <400> 99
                                                                         60
qtccnqqacc qatqttqcna aqanntttct tqqtccanta qgttcnaaaa aatgataanc
naggtntanc acgtgaagat ntntatanag tcttantnaa aacncntaga tctgnatgac
                                                                        120
gataantcga anacnggggg aggggntgag gngaggtggn gtganggaag anntgttgat
                                                                        180
                                                                        207
aaaagannna gntgataaga anngagc
      <210> 100
      <211> 200
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(200)
      <223> n = A, T, C or G
      <400> 100
acntnnacta gaantaacag ncnttctang aacactacca tctgtnttca catgaaatgc
                                                                         60
                                                                        120
cacacacata naaactccaa catcaatttc attgcacaga ctgactgtaa ttaattttgt
                                                                        180
cacaggaatc tatggactga atctaatgcn nccccaaatg ttgttngttt gcaatntcaa
                                                                        200
acatnnttat tccancagat
      <210> 101
      <211> 51
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(51)
      <223> n = A, T, C or G
      <400> 101
tcgagcggcc gcccgggcag gtctgaccag tgganaaatg cccagttatt g
                                                                         51
      <210> 102
      <211> 385
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(385)
      <223> n = A, T, C or G
      <400> 102
```

```
aacgtggtcg cggccgaagt ccatggtgct gggattaatc cactgtgacn gtgactctga.
                                                                        60
gttgagttgt ttttcaatct tctccaagcc tgtggactca tcctccacat ccttgggtag
                                                                        120
                                                                        180
taggatgaac atgctgaaga tgctnatttt gaaaaggaac tctatgaatc ttacaattga
                                                                        240
atactgtcaa tgtttcccca tnacagaacg tggnccccca aggttccatc atctgcactg
                                                                        300
ggtttgggtg ttctgtcttg gttgactctt gaaaagggac atttcttttt gttttcttga
                                                                        360
attcanggaa attttcttca tccactttgc ccacaaaagt taggcagcat ttaaccccca
                                                                        385
anggattttg ggtctgggtc cttcc
      <210> 103
      <211> 189
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(189)
      <223> n = A, T, C or G
      <400> 103
                                                                        60
agcgtggtcg cggccgaagt ctgcagcctg ggactgaccg ggaagctctg attatttacc
                                                                       120
caccacaggt angttgtgtt ctgaatctca agttcacagg ttaaggctac agcatcctca
                                                                       180
tectecaegg ggttggantt gttgetggtg atgaanggtt tggggtgget etgeataact
                                                                       189
gttgatctc
      <210> 104
      <211> 181
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(181)
      <223> n = A, T, C or G
      <400> 104
tegageggee geeegggeag gteeaggtet ecaceaange aceaeegtgg gaagetggta
                                                                        60
                                                                       120
attgatgece acettgaage enntggggea ecateeneea aetggatget gegettggtt
ttgatggtgg caatggcaca ttgactcttt tgggaaccac ttcaccacgg tacaacaggc
                                                                       180
                                                                       181
      <210> 105
      <211> 327
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(327)
      <223> n = A, T, C or G
      <400> 105
tegageggee geeegggeag gtettetgtg gagtetgegt gggeategtg ggeagtgggg
                                                                        60
ctgccctggc cgatgctcan aaccccagcc tctttgtaaa gattctcatc gtgganatct
                                                                       120
ttggcagcgc cattggcctc tttggggtca tcgtcgcaat tcttcanacc tccanaatga
                                                                       180
anatgggtga ctanataata tgtgtgggtn gggccgtgcc tcacttttat ttattgctgg
                                                                       240
                                                                       300
ttttcctggg acagaactcg ggcgcgaaca cgcttanccg aattccaaca cactggcggg
                                                                       327
cgttactagt ggatccgagc tcggtac
```

```
<210> 106
      <211> 268
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(268)
      \langle 223 \rangle n = A, T, C or G
      <400> 106
agegtggteg eggeegangt etggegtgtg ceacateggt eccaeetege tttacaaaac
                                                                         60
agtcctgaac ttnatctaat aaaattattg tacacnacat ttacattaga aaaaganagc
                                                                        120
tgggtgtang aaaccgggcc tggtgttccc tttaagcgaa ngtggctcca cagttggggc
                                                                        180
atcgtcgctt cctcnaagca aaaacgccaa tgaaccccna agggggaaaa aggaatgaag
                                                                        240
                                                                        268
qaactgnccn gggangnccg ctccgaaa
      <210> 107
      <211> 353
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(353)
      <223> n = A, T, C or G
      <400> 107
tcgagcggcc gcccgggcag gtggccaggc catgttatgg gatctcaacg aaggcaaaca
                                                                         60
                                                                        120
cctttacacn ctagatggtg gggacatcat caacgccctg tgcttcagcc ctaaccgcta
ctggctgtgt gctgccgcag gccccagcat caagatctgg gatttanagg gaaagatcnt
                                                                        180
                                                                        240
tgtnnatgaa ctgaancnta aattatcagt tccannacca ngcaaaaacc acccngtgca
ctccctggcc tggtctgctg atgggacctc gggcgcgaac acgctnancc caattccanc
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nectgectee caectatete tecenaatta taaacageet eettgggaag cageagaatt
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taaaaactct cccnctgccc tnttgaacta cacaccnacc gggaaaacct ttttcanaat
                                                                        240
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ggcacaaaaa tncnagggaa tgcatttcca tgaangaana aactgggtta cccaaaatta
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ggtacatgga tctcagcccc tgatggacac ggaacaggtg tggtcagaac tcccangatt
ctgcatccan gatccagtct ctatagaagt tatggatcat tccttcattt cattccccc
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ttcatgaaaa aacttctgaa caagcctttt ttctcacttt ggggccctgt ttggcncaag
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tgctgctcac ttccttaccc agggaatata ctgcataagt ttctgaacac ctgttttcan
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tattcactgt tcctctcctg cccaaaattg gaagggacct catttaaaaa tcaaatttga
                                                                       240
atcctgaaan aaaaacngga aatntttctc ttggaatttg gaatagaatt attcanttga
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acctta
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aaaggtcaat tgttcnccnc atgaaanaag ataaattgtt catccatcac tnctgaacca tccaaaacgc cggcggaatt attnccccgt tattatgggg aacggaattt tnaataaatt tgggaangaa tggggctttt attgttttgt tttccccctt tcttggcatt gattgggccg caatgggccc cctcgctcan aanntgcccc ggggccggcc gctccaaaac cgaaattccc anccacactt ggcgggccgt tactanttgg atccgaactc ggtta	180 240 300 360 405
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nggaaacagg natcagcatg anggtancan aaaccttatn accnangege acganetgae
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                                                                        240
ttetteeaaa gagttgnggt teegggeage ggteattgee gtgeeeattg etggaggget
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nacatgtcct atttagttat tcaaatacca gttgagggca ttgtgattaa gcaaacaata
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                                                                        240
                                                                        300
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120

180

240

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301

2280

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		35		Ser	_		40	_	_			45			
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	_		_	Cys 85		_	_		90			-		95	_
			100	Leu				105		_			110	_	
		115		Thr			120	_		_	_	125			
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Ser	Asn	Val	Asn	Ile 165	Glu	Leu	Leu	Asn	Ala 170	Leu	Arg	Tyr	His	Met 175	Val
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		195		Asn			200					205			_
	210			Asn	_	215					220				
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_		275		Leu			280					285		-	
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				Leu 325					330					335	
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See Ram Lys Rap Ie Leu Ala Thr Sam Gly Val Ile His Tyr Ile Rap 365 365 365 365 365 365 370 375 380 380 390 395 395 395 3																
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Solution					485					490					495	
S15				500					505					510		
S30			515					520					525			
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S80	_				565					570					575	
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Val His Val Ile Thr Asn Val Leu Gln Pro Pro Ala Asn Arg Pro Gln 625 630 635 640 Glu Arg Gly Asp Glu Leu Ala Asp Ser Ala Leu Glu Ile Phe Lys Gln 645 655 Ala Ser Ala Phe Ser Arg Ala Ser Gln Arg Ser Val Arg Leu Ala Pro 660 665 670 Val Tyr Gln Lys Leu Leu Glu Arg Met Lys His 675 680 <pre></pre>			595					600					605			
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<210> 134 <211> 234 <212> DNA <213> Homo sapie	en .				
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<210> 137 <211> 269 <212> DNA <213> Homo sapien				
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<210> 138 <211> 452 <212> DNA <213> Homo sapien				
<220> <221> misc_feature <222> (1)(452) <223> n = A,T,C or G				
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      <213> Homo sapien
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atattcctcc acaaaccact gtaccatatt accttatttt atcttcttga aattcttatt
                                                                       120
cattggcttg tttgttgtct ctttgcatta gatatatgta agctccttgg cataaatttg
                                                                       180
acattggtag gggactgaca ttctaacctg gcccaggccc taggagagag ataactccac
                                                                       240
aaagcagcac atactatctt aggttagcag ggagctaact caccatgtag cagatgaaaa
                                                                       300
aaaccaaacc cagcactgtg cataaatacc acttgccaag aagtcaggtc ctcggcaacc
                                                                       360
gagaatcaac ctcagcacaa acgcaggtgg ctgggctctg ttccccctta gccaccacct
                                                                       420
cagcetetee ceteceetge eccaagtgee caagagettg getetetgtg ettt
                                                                       474
      <210> 140
      <211> 487
      <212> DNA
      <213> Homo sapien
      <400> 140
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tgcaggggat ggcactttga gccctctgga gccctcccct tgctgagcct tactctcttc
                                                                       120
agactttctg aatgtacagt gccgttggtt gggatttggg gactggaagg gaccaaggac
                                                                       180
actgacccca agetgtectg cetagegtec agegtettet aggagggtgg ggtetgeetg
                                                                       240
tectggtgtg gttggtttgg ceetgtttge tgtgactace ecececete ecegaaceqa
                                                                       300
gggacggctg cctttgtctc tgcctcagat gccacctgcc ccgcccatgc tccccatcag
                                                                       360
cagcatccag actttcagga agggcagggc cagccagtcc agaaccgcat ccctcagcag
                                                                       420
ggactgataa gccatctctc qqaqqqcccc ctaataccca aqtqqaqtct qqttcacacc
                                                                       480
ctggggg
                                                                       487
      <210> 141
      <211> 248
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A, T, C or G
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tcaggtcagg tagagtcaaa atcaggcacc ccgactcaca gactgcttca cattgccatc
                                                                       120
agagattgtc ctgcaacaat attatgttta gttctactgc agaatgataa ctggatctta
                                                                       180
ccccctttgc ctgatctggc cacaaacttg tttttcaggt ctttccatta ggctctcttc
                                                                       240
agctaatt
                                                                       248
      <210> 142
      <211> 173
      <212> DNA
      <213> Homo sapien
      <400> 142
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                                                                        60
togtattaaa agtttctact toottgtaga atatotacat ocaatgggoo atggcacaaa
                                                                       120
atttaagtct agaaagaatc ttaaaggctc atcttatagt aaccagaggc agg
                                                                       173
```

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<211> 511
      <212> DNA
      <213> Homo sapien
      <220>
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      <223> n = A, T, C or G
      <400> 143
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                                                                         60
ttcagggcag agggaatgag gcaacccagt ggcagccccg ctgggccccg tggctcctgc
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tctcctattg gacgtagagg caggggagag acttctctat acaaatattc tcatcacaga
                                                                       180
agggatgate cttgctgctc tgccgtaggg tttttgatgc tgagctatgc tgcacatgac
                                                                       240
gttaacctaa agaacttgga ctgagctttt aaaaaaggac agcaaacaat tttataatcc
                                                                       300
ttaaagtgta atagacggtt acactagtgc agggtattgg ggaggctctt tgggtgtgga
                                                                       360
                                                                       420
ggctgtcact tgtatttatt gtgactctaa atctttgata gtaaaacaaa tgtaaaaaga
                                                                       480
aatgtttgcc accagatggg aatagaagtt ccaataagca ggctggaatg ggtggctata
cgttgtatca cgaggaagtt ttagactctg a
                                                                       511
      <210> 144
      <211> 190
      <212> DNA
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      <400> 144
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agacttccgc tacacttttc acaaaattat ctccaggtat cttctctgcc aagcagatgt
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caagagtggg aatggtcagg ctggggtaca gcctgctctc ggtgtgggcc tatgatctag
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gctctcgcct
                                                                       190
      <210> 145
      <211> 169
      <212> DNA
      <213> Homo sapien
      <400> 145
                                                                        60
gatgtggtta tctcctcaga tggccagttt gccctctcag gctcctggga tggaaccctg
                                                                       120
egectetggg ateteacaac gggcaccacc acgaggegat ttgtgggcca taccaaggat
                                                                       169
gtgctgagtg tggccttctc ctctgacaac cggcagattg tctctggat
      <210> 146
      <211> 511
      <212> DNA
      <213> Homo sapien
      <400> 146
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cagggaaga't gactagattt cctaacatcc atgagtgaaa tttatagaag tatactctct
                                                                       120
gacttgatat aaaggaagat tttaaaaaac atgactgttc aggagtgttc aagtagggtc
                                                                       180
                                                                       240
agatgaccag tgattgggaa tacttcgtaa gcaggagcaa gtaagatctg agccactgtt
                                                                       300
ctatcggtag ggtgtctgtg gtattccttg gtcaaagaag tactctaagc aacttcagtc
                                                                       360
tcacgaatta ctatcaccct cgtgggcata catgatggtt accctaaaga ggaagtttca
gaaggcagta atattggatc ctggaatagt cagacaggag ccttcatgca gatacccttt
                                                                       420
tcagttctcc atacacccat tcacaagtgg tcacaaaaac acccagtacc tttacttggc
                                                                       480
tttacccact taacaatatg ctcaatatga g
                                                                       511
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      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(421)
      <223> n = A,T,C or G
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ggccagttag caacacaggg agaatctgcc tgaactgacc aaaggtgtcc atacttcatg
                                                                       120
tcagtgagaa tttcacctcc atcatgttct aaagagccaa caacagattc tagggcactg
                                                                       180
                                                                       240
caaaatgctt cagcaattaa ttgaagttct gtttgagtac attcatcatc tttgagaatg
ctttctgggt cgttgtgagt cttgtgtctg atatatgcag ccaaatgagt ttcagtacag
                                                                       300
                                                                       360
ccacctccca acaaagccca tggttccttg agtgttaact gcaggacatg cagtgccgtc
                                                                       420
tgacacgtga gcttcagctc atcccangca gtgtcatttc tgttgcagag aagccaagct
                                                                       421
g
      <210> 148
      <211> 237
      <212> DNA
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      <400> 148
acacaccact gttggccttc catctgggtt aagtcaactg tgagtagaaa ccgaagataa
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cagttttgta ttcataatgg ccttttcata ctccaagtac ttttgagcac agagcctctt
                                                                       120
                                                                       180
gettetgace tggcacttgg aacacagata tatatatett ttgttetgte cetgggaaac
                                                                       237
tgatatttqt qtaaqacaac caccaqatat tttctctaat aaaatcttct aaaatta
      <210> 149
      <211> 168
      <212> DNA
      <213> Homo sapien
      <400> 149
                                                                        60
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ataagataaa ettttttgte tttgetttat ettattaggg agttgtatgt eagtgtataa
                                                                       120
aacatactgt gtggtataac aggcttaata aattctttaa aaggagag
                                                                       168
      <210> 150
      <211> 68
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(68)
      <223> n = A, T, C or G
      <400> 150
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                                                                        60
                                                                        68
ggaaattt
      <210> 151
      <211> 421
      <212> DNA
      <213> Homo sapien
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<400> 151			•		
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<210> 152 <211> 507 <212> DNA <213> Homo sap	oien				
<220> <221> misc_fea <222> (1)(! <223> n = A,T,	507)				
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<210> 153 <211> 513 <212> DNA <213> Homo sag	pien				
<400> 153					
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<213> Homo sapien

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<210> 156 <211> 509 <212> DNA <213> Homo sapien				
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<210> 158 <211> 507 <212> DNA <213> Homo sapi	en				
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<210> 159 <211> 508 <212> DNA <213> Homo sapid	en				
<220> <221> misc_feator <222> (1)(500) <223> n = A,T,C	3)				
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<211> 508 <212> DNA <213> Homo sapie	en				

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      <222> (1)...(508)
      <223> n = A, T, C \text{ or } G
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gaaaaccaac aaataattaa tcaaatacaa gaatctcatg ctgaaattat ccaggaaaaa
                                                                       180
                                                                       240
gaaaaacagt tacaggaatt aaaactcaag gtttctgatt tgtcagacac gagatgcaag
                                                                       300
ttagaggttg aacttgcgtt gaaggaagca gaaactgatg aaataaaaat tttgctggaa
                                                                       360
gaaagcagag cccagcagaa ggagaccttg aaatctcttc ttgaacaaga gacagaaaat
                                                                       420
ttgagaacag aaattagtaa actcaaccaa aagattcagg ataataatga aaattatcag
                                                                       480
gtgggcttag cagagctaag aactttaatg acaattgaaa aagatcagtg tatttccgag
                                                                       508
ttaattagta gacatgaaga agaatcta
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      <211> 507
      <212> DNA
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                                                                       180
cagtagcctc ggcccaagag gcctgctttc cactcgctag ccccgccggg ggtccgtgtc
ctgtctcggt ggccggaccc gggcccgagc ccgagcagta gccggcgcca tgtcggtggt
                                                                       240
                                                                       300
gggcatagac ctgggcttcc agagctgcta cgtcgctgtg gcccgcgccg gcggcatcga
                                                                       360
gactateget aatgagtata gegacegetg caegeegget tgeatttett ttggteetaa
                                                                       420
gaatcgttca attggagcag cagctaaaag ccaggtaatt tctaatgcaa agaacacagt
                                                                       480
ccaaggattt aaaagattcc atggccgagc attctctgat ccatttgtgg aggcagaaaa
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tgaaaaattg tctttcctta tcattggtgg gaggcttggt agcaaagtaa cattttttgg
aaaagaggac agaaaaattg aactacagct tgagaacgta ttcttttttt cctactttgt
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tattgcaaat tgaggaatca cttttaactg ttttaggtgt gtgtgtccag agtgagcaag
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                                                                     120
atattaaaaa ggaaactaat tggaccattt tctatttgtc tattttatac aaaaaggcta
                                                                     180
                                                                     240
cacaattqtt acactttatt cagattacaa ttaattagag tgattatgaa ttagtgttct
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acaccattac tcaattctta aaaattagaa attgctgtag cagtattcac tataacttaa
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cactacgaga gacttaaaaa acagttactg caaaaaaaaa aaagagctac ttcaaagcaa
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attcatgtat aacttggatc acacaccagt atataacgac aaaagataaa tgtataataa
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                                                                     240
aaagattgga taaatcagaa gaggcttttt ggtcttgaat tcttcaccca ctaacaatga
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agcagcactg taggcagccc aaaacacacc aaacagtttt ataagtgtag acaccacttc
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aaatqatcca accaccaaaa qtacaqqqqc tattacaatg agaggaagta atgaatatcc
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tataactcca aggacttgg
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     <211> 387
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                                                                     120
agaagggtaa ctcggctaca gtaacagctt aattttgtta aatttgttct ttatactgga
                                                                     180
qccatgaagc tcagagcatt agctgaccct tgaactattc aaatgggcac attagctagt
                                                                     240
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ataacagact tacataggtg ggcctaaagc aagctcctta actgagcaaa actgagcaaaaa actgagcaaaaa actgagcaaaaa actgagcaaaaa actgagcaaaaa actgagcaaaaa actgagcaaaaa actgagcaaaaaaa actgagcaaaaaaaaaa	00 60 37
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<210> 257 <211> 420 <212> DNA <213> Homo sapien	
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<211> 450

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      <213> Homo sapien
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      <223> n = A, T, C or G
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                                                                       120
                                                                       180
attcaatttg gagctccttc cttttttata gcacttctaa gctgtgtgcg cgacacacac
                                                                       240
cacaqagqta qgaaqqacca cctttaataa attatcttct taatcgcaga gaatttctga
                                                                       300
agataaaact gacaaaatgc taaaccaagg ctttgatgag tcccaaagga ccacagatcc
                                                                        360
ateggeteet atttgaagaa tteateeeet gtagtgttet ageetttgta gggeaetgga
                                                                       388
ttacaagatc caccagggct ctgaacaa
     <210> 266
      <211> 616
      <212> DNA
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     <220>
     <221> misc feature
     <222> (1)...(616)
     <223> n = A, T, C or G
     <400> 266
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aagacaagct gaatacatat ctatgttctg aataagtcca ctatggatat atataggaag
                                                                       120
agatatacat atatccatcc acagatacac acacacatat atatttctgc atgtatatat
                                                                       180
acataattct ttctatagtt acaggaaata cttcttctat aattctgatt ttgactccca
                                                                       240
tcctccacca tttactcatc cactcattac ctaaatcttg gctttctttc ctatattgta
                                                                       300
aataatccat ccaaacttct agccagtact gtcaggaggg ttcttgctcg agtgagctgt
                                                                       360
taatactatt ttccactgac aacttctgca catcgaggac acagtgtatc tgaagactcc
                                                                       420
gctgtatact tccaacaacg ggggcatttt tctttcgtag tcggcatgac aattacttta
                                                                       480
taggaagact cttcacgaat atcaccacct tctaagttga tgaggaattt ccctttaagc
                                                                       540
togattacat ctgcagtcat ctctcgtggt tcctgaccag taaagttgac tcagaagcca
                                                                       600
                                                                       616
tcattaattc attcaa
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     <211> 341
     <212> DNA
     <213> Homo sapien
     <400> 267
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ttattcttgt tgtattgtca tttgagtttt gtatatattt ttgatattaa ccccttgtca
                                                                       120
catgtataat ttgcaaatat tttctccctt tttttagttg tcacattctg ttcattgtat
                                                                       180
cagattctgt gcagcagctt tttaatttga agtgatctga ctgacttgtt cttccttttg
                                                                       240
                                                                       300
tgtcctggga tatttaggtt aaatcaaaaa acttgctgcc cagaccaatg ttatggggct
                                                                       341
ttcactctat tttttggtag tagtagttta agagttttag g
     <210> 268
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<211> 367

<212> DNA

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<213> Homo sapien
     <220>
     <221> misc feature
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      \langle 223 \rangle n = A, T, C or G
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                                                                         60
                                                                        120
gacgtntcct tctagagagc aaatctatca taaaatgtca aaactagaag agaataaaat
                                                                        180
gaaaggaaaa aacctagaaa aatatcctaa aatatcaaat gcagtcattt ctaaatataa
gccataatta tagctttacc tattgttctt attgttccta tgctgcttct acaatgttac
                                                                        240
atcaactata cttagcttta ctctcccaaa atcttggtga tgaagccttc tgagtgtgct
                                                                        300
ttccaatgtg ccagaaccag aagggcattc caaggcttcc ccacatttcc tccatttacg
                                                                        360
                                                                        367
gagacag
      <210> 269
      <211> 270
      <212> DNA
      <213> Homo sapien.
      <220>
      <221> misc feature
      <222> (1)...(270)
      <223> n = A, T, C or G
      <400> 269
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                                                                          60
gnaangengn tgaggtggat taaaccaaac ccagctacgc aaaatcttag catactcctc
                                                                         120
aattacccac ataggatgaa taatagcagt tctaccgtac aaccctaaca taaccattct
                                                                         180
taatttaact atttatatta teetaactae taeegeatee etaetaetea aettaaaete
                                                                         240
                                                                         270
cagcaccacg accctactac tatntcgcac
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       <211> 368
       <212> DNA
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       \langle 223 \rangle n = A,T,C or G
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ttgccccata cccttagatt atgtcagact aaagctgaca attctgccag gctctgaacc
                                                                         120
 cctagtgccc ccaacccaaa tcttggaagc aaagaatatg ccctgtcata caactttgta
                                                                         180
 caagttgtag taaaacaaag cttaagtttt ctcatctttc tacagcaaat ggtcagttat
                                                                         240
 ttaataaaca ctaaaatgct cctaagaatc cattttgagt ttgtttacca aacacattgt
                                                                         300
 gcaagaactg actacacaaa aagtteettt gaaatttggt ecacaaatte acttaaggtt
                                                                         360
                                                                         368
 ggaaattt
       <210> 271
       <211> 313
       <212> DNA
       <213> Homo sapien
       <220>
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<221> misc feature
      <222> (1)...(313)
      <223> n = A, T, C \text{ or } G
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                                                                         120
agacaanngt ttgcaaacac atgtccaatt caggaaaaaa aatttcacgt ttctcgtctg
gettttttet tetttttat ttgtttggga gatteceage tagttteaga ettggtetgt
                                                                         180
gaaggaggca cactattttg cttggtattt gacttggatt tatctgtctc ttgtagtatt
                                                                         240
ggcggcactt gggaagagct cttgtcagaa tcactttttg ataagattac agatggctcg
                                                                         300
                                                                         313
gtagaagtag cag
      <210> 272
      <211> 462
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(462)
      <223> n = A, T, C or G
      <400> 272
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tacaaaatct atatacttgc acatttagta tttgtcaatg tgccagaggt tttcttcatg
                                                                         120
                                                                         180
aaatttgact tctttgaagt gaaggetttt ttetateate tettataget etgactgaat
                                                                         240
aagtettaat getttettea tgttttetat caataggggt aaateeegag geteatatgt
gtacaatctq ttaqagtatc ttccagctat gtcagctcta actgttaaag aagggtctac
                                                                         300
aaacatqatt ctaqqcacat attqcccatc aqqtqataaa ttcttatcag tggtttcatg
                                                                         360
                                                                         420
cataaggttt agcatgatga acttattctg agccatttct tgtatttctt cattttgggc
aaatactttc tttagtgctt gagagtattg acaatcctcc ag
                                                                         462
      <210> 273
      <211> 282
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(282)
      <223> n = A, T, C \text{ or } G
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ctgatcaaag catgggatat tttaatagtn ttatacataa tatttttaca tagaaaactt
                                                                          60
tacatnncat ttcatattat ataattctgc ttattctttc aaaaatttat acatccattg
                                                                         120
ggcaaggaat ggttttcatt aaattaccaa tattaaatgc acttaatcat tgtgtatagg
                                                                         180
ttaaaccaaa gtaactatta actaactttt aggcatttta aggaggtaaa acatacattt
                                                                         240
                                                                         282
tacacataag tatttgatgc aaatatgcag ataaaatttt tt
      <210> 274
      <211> 125
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(125)
      <223> n = A, T, C \text{ or } G
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<400> 274
cagccctaga cctcaactac ctaaccaacn ttncttaaaa taaaatcccc actatgcaca
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ttnaatcnct ccaacatact cggattctac cctagcatca cacaccgcac aatcccctat
                                                                        120
                                                                        125
ctagg
      <210> 275
      <211> 528
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (528)
      <223> n = A, T, C \text{ or } G
      <400> 275
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ataagccngg aaccacaaat aattaaaagg aaacacagca atcccataaa caagcattct
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ggcatctgtt agaaattttc cctcaaatta tgaaatgtag ctctccatgc tttccaatga
                                                                        180
ttgttataat acccacaaat atctgtgatt tcagtggaat actttaacaa aagttttctt
                                                                        240
tttaaggcat gatectgatt cattittet teaatatete agteatttea ggaactacet
                                                                        300
taaataaatc tgcaactatt ccataatctg ccacttggaa aattggagct tctgggtctt
                                                                        360
tattaattgc cacaattgtc ttgctgtctt tcatcccagc taaatgttgg atggctccag
                                                                        420
atattccaac agcaatataa agttctggtg ctactatttt tcccgtctgn ccaacttgca
                                                                        480
                                                                        528
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       <210> 276
       <211> 420
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(420)
       <223> n = A, T, C \text{ or } G
       <400> 276
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agaaacctga taaaatatac ttttgtgaac aaaaattgag acatttacat tttctcccta
tgtggtcgct ccagacttgg gaaactattc atgaatattt atattgtatg gtaatatagt
                                                                       180
                                                                         240
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gttatattac caagactttg actagaatgt cgtatttgag gatataaacc cataggtaat
                                                                         300
aaacccacag gtactacaaa caaagtctga agtcagcctt ggtttggctt cctagtgtca
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                                                                         420
       <210> 277
       <211> 668
       <212> DNA
       <213> Homo sapien
       <220>
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       <223> n = A, T, C or G
       <400> 277
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aaatttaaag ggaaaaccct caggcctgag gtgtgtgcca ctcagagact tcacctaact
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agagacaggc aaactgcaaa ccatggtgag aaattgacga cttcacacta tggacagctt
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ttcccaagat gtcaaaacaa gactcctcat catgataagg ctcttacccc cttttaattt
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qtccttqctt atqcctqcct ctttcqcttq qcaqqatqat qctqtcatta qtatttcaca
agaagtagct tcagagggta acttaacaga gtatcagatc tatcttgtca atcccaacgt
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                                                                        540
tttacataaa ataagagatc ctttagtgca cccagtgact gacattagca gcatctttaa
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cacaqccqtq tqttcaaatg tacaqqqtc cttttcaqaq ttgqacttct agactcacct
qttctcactc cctqttttaa ttcaacccaq ccatqcaatq ccaaataata gaaattgctc
                                                                        660
                                                                        668
cctaccag
      <210> 278
      <211> 202
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(202)
      <223> n = A, T, C or G
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ttngcnaagt ggggtcccat caaggttcag tggcagtgga tctgggacag atttcactct
                                                                        180
cacqatcagc agtctgcaac ccgaagattt tgcaacttac tactgtcaac agagttacat
                                                                        202
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                                                                        120
qaqaaqtaaa taaaqccaat qqcactccct tcaqaqqctc aaaatqqtta qattttqatq
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cagatttaac cttagcgagt ttcagtcagt ccatttagat gatcctgtag gttcatacaa
                                                                        240
atacactgaa ccqttqqttt aacttctctt ccttcctcaa aqtttatqat aaaqaqactc
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atccctgtat tgggagtgac tgacataagt tcagatctgc tcagagtggc tggtaaggaa
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cacttaaggt cagtcagaaa ataatcaaac agacttctca tgtaagcacc gtgactcaca
                                                                        420
actaagacac tggctgctaa tcctggaata ccgctgtctg aattaacttt agagctgtga
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ttttttccta aaggaaatat ctctgccaaa gaagtttcca gacagntgct tgggagatcc
                                                                       540
ttqqqqaaaa ctqqtctttt tqatccqqtt ctttcanqan taqqtnqaca aaaqaaatnc
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aaaaaagnct atcccacgcn tttntcacct gggcccagcg gnnctcctcc nggggggggn
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<210> 284 <211> 288 <212> DNA <213> Homo sapien	
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<210> <211> <212> <213>	340	en		,		
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cgcaatttta ccttctgtct tttcagctac ccaggtgttt atgtgttttc tggacttctc
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tacggcgctg ataaagtcaa gctcctccat ctctgcttgg tagaattttt ggcaggaate
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                                                                       290
totaaaagat gagaggaaat cacaagactt ttccccaaag agcctgttgg
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      <212> DNA
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                                                                        120
accagaatct tgcacagctt ttggtgtttg gatcatagta ccattttaat atgaaatccc
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tgcaagttcc ttcgtctttc ggcaacttgc atatatctgt ttcagtgaga gccaatggtt
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ctgtgctcac cattagattg atggttgaac tagaagctga ccttgctggc tgtggaggtg
                                                                        300
ggggctgaga tttctttgta ctgaaacttc cgtggtaggt ggctctgacc tgagacctca
                                                                        360
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 cetecateca gttgttgaag ggtgcagece gettggcata etecaagtae agetggteaa
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 tggtetecag cagitteteg giecgeteca gagetteeet tegettetga gitagggeee
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 ccagattgtc ccactggtca cagatctttt ggcaacgggc gttgacactg ggtgagtcat
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 aatantccag ctcattgagc tcctgtgcga tggcggcaat ctgctccaca cggtcctggt
                                                                        360
                                                                        384
 gggcagccag gccactctcg aagg
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       <211> 278
       <212> DNA
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 gtaaatacta tatgttgaac aaattaaatg tcaaaatttt ttattaccat agtccatgtt
                                                                         120
 aatagtgggg ctttcaggtg tttagagatt ttttttgttg ttgttaacat tcattgcaaa
                                                                         180
 agtactagat ggtgtataac tctagagttg aattttaagg gattccctaa tatgtatact
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                                                                         278
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cetecgttte etgettaagt geatteegtg caategtetg gaacgeetge tecaegttga
                                                                  120
                                                                  177
tggcctcctt ggcactggtc tcaaagtagg gaatgttgtt tttgctgtag caccagg
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     <211> 403
     <212> DNA
     <213> Homo sapien
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                                                                  120
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cagtactgtt ggttaaatga caatttatgt ggattttgca tgtaatacac agtgagacac
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agtaatttta totaaattac agtgoagttt agttaatota ttaatactga otcagtgtot
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                                                                  300
gcctttaaat ataaatgata tgttgaaaac ttaaggaagc aaatgctaca tatatgcaat
                                                                  360
ataaaatagt aatgtgatgc tgatgctgtt aaccaaaggg cagaataaat aagcaaaatg
                                                                  403
ccaaaagggg tcttaattga aatgaaaatt taattttgtt ttt
     <210> 294
     <211> 305
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                                                                  180
agtattcagg cagatgttac ataactgcta attaagtttc cctggattga ntttanncaa
                                                                  240
                                                                  300
anaattgaaa gtngattttg gtcangtgtc agnaaactac tgcctataaa cccatatent
                                                                  305
accca
     <210> 295
     <211> 397
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
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caattatgcc aaaagacatc cagctagcac gccgcatacg tggagaacgt gcttaagaat
                                                                  120
180
cctgttattg gtagttctga acgttagata ttttttttcc atggggtcaa aaggtaccta
                                                                  240
agtatatgat tgccgagtgg aaaaataggg gacagaaatc aggtattggc agtttttcca
                                                                  300
tttncatttg tgggngaatt tttaatataa atgcggagac gtaaagcatt aatgcnagtt
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aaaatgtttc agtgaacaag tttcagcggt tcaactt	397
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<210> 297 <211> 681 <212> DNA <213> Homo sapien	
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gaaagaaagc aggctaggca tgtgaaatca ctttcatgga ttattaatgg atttaagagg
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gcatcaatca gctcaactca agatttcata atcattttta gtatttagat tgtgcctcaa
                                                                       240
                                                                       300
agttgtagta cctcacaata cctccactgg tttcctgttg taaaaacctt cagtgagttt
gaccattgtg ctcttggctc ttgggctgga gtaccgtggt gagggagtaa acactagaag
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totttagtac aaaactgctc tagggacacc tggtgattcc tacacaagtg atgtttatat
                                                                       420
tteteataaa gagtetteee tateeeaagg tetteatgat geeagtagee atatatgata
                                                                       480
aattatgttc agtgataact tagttatcag aaatcagctc agtggtcttc cccgccatga
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cacttggcac acaggtttgt atgtatgtgt atatatatat gtatg
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      <211> 438
      <212> DNA
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ttagcacaat ttgagactga aatttagtac actatgttct aggtcagtct aacagtttgc
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ctgctgtatt tatagtaacc attttccttt ggactgttca agcaaaaaag gtaactaact
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gcttcatctc cttttqcqct tatttqqaaa ttttaqttat agtqtttaac tqqcatgqat
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taatagagtt ggagttttat ttttaagaaa aattcacaag ctaacttcca ctaatccatt
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atcctttatt ttattgaaat gtataattaa cttaactgaa gaaaaggttc ttcttgggag
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tatgttgtca taacattt
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accacaagtc caattgctat ggttacttca ggaagctgag gaactggtct gatgccgagc
                                                                       120
tcgagtgtca gtcttacgga aacggagccc acctggcatc tatcctgagt tt
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tttcaaatgc cacgctgacg tcacgcctgg cctgaaattt cacatcacta acatctgacc
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ggatgagcct ctaaaaataa aacaatcttt agacgatcca gactaatgga aggacagaga
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                                                                        313
ggttgattac ttt
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      <211> 366
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catttataag tcagcatcca aggtaaaaga attctctgtt ggacttgaca tcactcccat
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cctctgatac tcgcctactc tcttctcaaa gaagttagnt ctttccttcc antgaaatat
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tetcataaaa gtcaaatggg ttetetacte tgaaaacett getaaaacec aattecagea
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taagtttgtc tgncacaaac ncaatgnatt gcttcattaa antgcaattc atcccaatga
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gcttcc
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                                                                        120
ctgatgtccc ggatgccatc atataccagg cgggaagcat cgataaactc attctcatcc
                                                                        180
atgggctggg cagggtccga gctgagggct tccacggctg cttctacttg ctcagtaaaa
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cgtggcatga ctgtgttgga gagcagctta gtggcttcca gaaccttctc tgtgtagact
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cctggctcat agtcgtccat ctctgaggtg actacgtgaa tgacccgggc tgcccggcct
                                                                        360
cgaattgcac cagctgtgcg gccaggccat ccacatcctt ctcttggaga gcaatgacac
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atttggtcac atcttccaaa atgtgattct ctgagacagc caagaagtca tcaatggaag
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92

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tacataacac caattaatga gatcattact gctttatgct ctaattgctt cctgtattca aaatcttctc tccaaccaca taatgactcc ctaaacttct cttgtatttt ccaatgactt gtacaagcac agaactggtc aatcaataaa tactcactgg ttatttgagg aaaaaaatgtt gccaagcacc atctttatca gaaaataaat caattcttct aaacttggag aaatcaccct attcctagta tgtgatctta attagaacaa ttcagattga gaangngaca gcatgctggc atttgaggag cccttcagcc t	420 480 540 600 660 720 741
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180
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tgctgttgtg tgcgttgagc ctggtcggct gtgggaggtg gtggattctt cactgacgcc
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gctgctgtgg gaagttgtag aatgccgact gaggcctgcc gtggtggtgc tgntagggaa
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tgctgctagc g
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cgtcggttcc cagccccttc atggaagctt ttagctcaga agcgtcatac tgagcaggtg
                                                                        180
                                                                        240
tetteaataq geceaaaate acegteteea ggtggecaga taaggetgae tteagtgetg
                                                                        300
atgcaagttc ctttttggtc cttctctggt aggcgaaggc aatatcctgt ctctgtgcat
                                                                        360
tqctqcqqtt qqtcaaaatg ttqacaatgg tqacctcatc cacacctttg qtcttqatgg
ctgtttcaat gttcaaagca tcccgctcag catcaaagtt agtataggct ttgacagacc
                                                                        420 ....
                                                                        476
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aaatatgtta aggattgaga cccaccaatg cactactgta atatttcgct tcctaaattt
cttccaccta cagataatag acaacaagtc tgagaaacta aggctaacca aacttagata
                                                                        240
taaatcctac caataaaatt tttcaqtttt aagttttaca gtttgattta aaaacaaaac
                                                                        300
agaaacaaat ttcaaaataa atcacatctt ctcttaaaac ttggcaaacc cttccctaac
                                                                        360
                                                                        420
tgtccaagtn tgagcataca ctgccactgg ctttagatac tccaattaaa tgcactactc
                                                                        455
tttcactggt ctgaatgaag tatggtgaaa caagc
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                                                                       120
                                                                       180
ggettetagt gaageeteet cacagtagge tteactagge ceacagtgee ectagaeete
tgacaatccc accctagaca gactttattg caaaatgcgc ctgaagaggc agatgattcc
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                                                                       297
caagagaact caccaaatca agacaaatgt cctagatctc tagtgtggna gaactat
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      <211> 144
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tgctagacct ggcatttgct cggc
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tgattcttta aatgtcttgt ttcccagatt tcaggaaact ttttttcttt taagctatcc
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aaaa
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catgggacta aatgaactaa tgaggataat attttcataa ttttttattt gaaattttgc
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tgattcttta aatgtcttgt ttcccagatt tcaggaaact ttttttcttt taagctatcc
                                                                        240
acagcttaca gcaatttgat aaaatatact tttgtgaaca aaaattgaga catttacatt
                                                                        300
ttctccctat gtggtcgctc cagacttggg aaactattca tgaatattta tattgtatgg
                                                                        360
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taatatagtt attgcacaag ttcaataaaa atctgctctt tgtatgac
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      <211> 455
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aactaactgn cnncttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt
                                                                        120
catgggacta aatgaactaa tgaggataat attttcataa ttttttattt gaaattttgc
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tganncttta aatgtcttgt ttcccagatt tcaggaaact ttttttcttt taagctatcc
                                                                        240
acagcttata gcaatttgat aaaatatact tttgtgaaca aaaattgaga catttacatt
                                                                        300
ttctccctat gtggtcgctc cagacttggn aaactattca tgaatattta tattgtatgg
                                                                        360
                                                                        420
taatatagtt attgcacaag ttcaataaaa atctgctctt tgtataacag aatacatttg
                                                                        455
aaaacattgg ttatattacc aagactttga ctaga
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                                                                        120
catgggacta aatgaactaa tgaggataat attttcataa ttttttattt gaaattttgc
                                                                        180
                                                                        240
tgattcttta aatgtcttgt ttcccagatt tcaggaaact tttttttctt ttaagctatc
cacagettae ageaatttga taaaatatae ttttgngaae aaaaattgag acatttaeat
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tttctcccta tgtgggcgct ccagacttgg gaaactattc atgaatattt atattgnatg
                                                                        360
                                                                        376
ggaatatagc attgcc
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      <211> 422
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                                                                        180
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ggagcgacca catagggaga aaatgtaaat gtctcaattt ttgttcacaa aagtatattt
                                                                        240
tatcaaattq ctqtaaqctq tqqataqctt aaaaqaaaaa aaqtttcctq aaatctqqqa
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aacaagacat ttaaagaatc agcaaaattt caaataaaaa attatgaaaa tattatcctc
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attagttcat ttagtcccat gaaattaatt attttctctg cttgatcttg gtggacagtt
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      <210> 386
      <211> 313
      <212> DNA
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<213> Homo sapien

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actatectge eggecateat ectagteete ategecetee catecetaeg catectttae ataacagaeg aggteaaega teeteett accateaaat caattggeea ecaatggtae 30	80 40 00 13
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ttcttatagg aataatgaac tgtcaaatgc catggcataa ttatttattt ccaagctatc
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atcaatgatt agaactaaaa aaaatttggc ataaaaaaat cacaattcag cataaataaa
gctattttta gcttcaacac tagctagcat ctctaagaat tgttgaaata agt
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      <211> 216
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      <213> Homo sapien
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gtctgaaaat gtaatatttt gataatactg taatatacct gtcacacaaa tgcttttcta
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atgctgaatt gtgatttttt tatgccaaat tttttaa
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                                                                        120
ttgacatgtg ccagggcaat gatgaatgag aatctacccc cagatccaag catcctgagc
                                                                        180
aactcttgat tatccatatt gagtcaaatg gtaggcattt cctatcacct gtttccattc
                                                                        240
aacaagagca ctacattcat ttagctaaac ggattccaaa gagtagaatt gcattgaccg
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cgactaattt caaaatgctt tttattatta ttatttttta gacagtctca ctttgtcgcc
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      <211> 373
      <212> DNA
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     <221> misc_feature
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     <223> n = A, T, C \text{ or } G
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                                                                        120
aatgagaatc tacccccaga tccaagcatc ctgagcaact cttgattatc catattgagt
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caaatggtag gcatttecta teacetgttt ecatteaaca agageactae atteatttag
                                                                        240
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ctaaacggat tccaaagagt agaattg ttattattat tttttagaca gtctcac ctcagatcag tgt	cat tgaccacgac ttt gtcgcccagg	tantttcaaa ccggagtgca	atgcttttta gtggtgcgat	300 360 373
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                                                                     180
tgcaaacatt atataaaaat agaaatacta actctacagg cagtatttcc tgataaatta
tttaaatagc atatctacac aatctgagat atctattcca atggcaatga gaaaataatt
                                                                     240
tataaaaata aagcaatggt ataccagatg atagaaaaaa acataacttt cagaaattgt
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atttaacatt tcaatgctat ttccttattg ggaatacttc tctgcagagt ttttatgcta
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tat
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ataaccattg ccccaccatg aacatggggc ttgggaagac agtcctacaa tcttcatcat
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ccgggcgcc cctaagggcg aattctgcag atatccatca cactggcggc cgctcgagca
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ctatattgag tggaattaca atncnct
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                                                                     120
180
ccacaaaaa aaaaaaaaa aaagtntata aaataaaata ttgaagtcct ttcccattaa
                                                                     240
aaaaaaaaa aagaaaaagc acggactctt tcatccagtt ctgatgtgat tatctctgga
                                                                     300
aggeattttc tectectett cectece
                                                                     328
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<210> 402 <211> 268

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      <220>
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      \langle 223 \rangle n = A, T, C or G
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ccaaggctgt ttcaagtagt cgaaagccat ccctggactg ttcaggtgcc ttttctattt	300
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tctgaaaagg agttgcatat ttccaaaaat aatattctta ttttaatcac acagaagaac gtggagcaca ggaaggaaat ggctgggtgg tcagagagag gtgagctgtc ggagaaacac	180 240
agttaaacta aaaaataaaa tccattttgt gtataaactg acttaaacgc atgcaaagaa	300
gtggaaaaca tatgccattt gtcaagaaaa atactgcttt atagctttta ctttacaatt aaaggagaaa gcagaggcca gatataagcc cagataataa catttaagtt tctcataaaa	360 420
ctcccaaatg t	431
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tcatctgtgt ccctaccacc tacaacaggc cagcaatcta cccgtgtgtg tttgttggac	240 300
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agtttgattg catataaatg tggaacttga tagatctcta tatttttaat gcacttgtga
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taaactggca gcagggttag acattacttt caaagcttga ggtagaccga gtcagcatgc
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tagacagget teteteteta accaaaactg
      <210> 446
      <211> 326
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cgtgacaggc tggaagagca aatgctgctg agcattctcc tgttccatca gttgccatcc
                                                                        120
actaccccgt tttctcttct tgctgcaaaa taaaccactc tgcccatttt taactctaaa
                                                                        180
cagatatttt tgtttctcat cttaactatc caagccacct attttatttg ttctttcatc
                                                                        240
tgtgactgct tgctgacttt atcataattt tcttcaaaca aaaaaatgta tagaaaaatc
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                                                                        326
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      <211> 304
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gaaacagett tagetteetg eteegaagge caaacacett ggetgettea tacagaagae
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cttggtgggt gagtccattc tgcccaagtg ggttttcaag caggagagtg cccactgtcc
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ccattaaaca ctcttgtggc tttgcattca ggagctgtag gttgatatac tgacaaggaa
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gagt
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                                                                        120
tgaagaatct ccatgggaga gattttttt cacccttcag aattatcttt ttcccctaag
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      <211> 481
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                                                                       120
aaagcttttt agtgatcatt tattactttg tgtttactag atattaattc taagatgaat
                                                                       180
                                                                       240
tcctttagaa ttttagaaaa aattattcta gacaacaatc aaagtaaagg atacatccag
cattgaaacc ataagccggc aagtctccag gttaaaaggt ttgtatcctc cagcaatgcc
                                                                       300
agactgtgtc agacatctct gcaattcatc agcatctatc tgcccatcct gtccagctac
                                                                       360
                                                                       420
agcagcaaag taaccataca gcggatcctg agtttgtccg ggaaacgcag gccctccggg
                                                                       480
agcccctcca tactqcatct tqaqttqaaq tcttatangt agaagctggt gatccttaga
                                                                       481
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aaacactcaa aacattttcc attggaaaca tgtaaagaca atatgaggtt ttgttaccat
                                                                       120
cttactgcaa ttttcttatg tgttactagt ctacataccc catgttttct gtaatcatgc
                                                                       180
agatgtgaat ggaagtttga atgattaaat aaatgaaaag tccgtttact gcagggaatc
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atttcacaag gcagccaaac cgggtttaga gaacaaaact attcaagaaa ttctcc
                                                                       296
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                                                                       120
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                                                                       180
cctttcctct cttttaaata attcttcatt qaqttctaat atgtaaaaaa aaagtttact
                                                                       240
gtaaagtttg caaataanga aattttttt aaaagtcctc agtaatctta ccagtaacaa
ttgttatggg cacatttgct tttggaagat ttcttttgta tgcatgggat aagt
                                                                       294
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      <400> 452
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tacaggtggc ctcagcttct aaacaccact acactgcttt atataaaaaa caaaaatcac
                                                                       129
atagaagag
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gaccttttta tgagaataaa atgtctattt ctgaaatgtc cctatttctg gaaatgttcc
                                                                        120
ttatactaaa gtccaacttg tgtggattan t
                                                                        151
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                                                                       120
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ccettttgtt ctgcttgcag ttggtcacat ctttctttct catggttaag ttctctttcc
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attctcccaa cttgttctcg aagttgtgct gtttcttttt ccagaacggc aattaacttt
                                                                       360
aacagttett ettttettt catggtttte teaattttea aeteaagaag geetgetttt
                                                                        420
                                                                        480
gtggtcacca ctaacatgtc agaatttcct tcatcttcca tagtaagcag ctcttcaact
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gagtagetca etgeteactg etgaggagaa aggeacaaga tataatgtea taagageagg
                                                                       120
acagtggctc agcctacaga gttccctata ggggaaagaa ggcaggaaat aggcgcaggg
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tetggteetg teeetgeace accetgagea getagtettg ggaagggatt acaggeeetg

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180
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qccgaacccg acatgcctct tgtccttggg gttcttgctg atgtaccagt tcttctgggc 420
cacactgggc tgagtgggt acacgcaggt ctcaccagtc tccatgttgc agaagacttt 480
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tttaagtgta actgagaatc cgttaaatat gcccttgtac ttttgggggt ccacctgcat 240
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gctgcggagg tccccgagac catcgtgcac canctgcaga tgtggcgtgt tgaaggggtt 480
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183
ccg
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tttgaaaaga aatttcagtc tgagaaggca gcaggctcgg tgtccaagag cacgcagttt 180
gagtacgcct ggtgcctggt gcggagcaag tacaatgatg acatccgtaa aggcatcgtg 240
ctq
                                                                     243
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teccagegae gaegeeaeeg egettatgae egaeeeeaag eteateaeet ggteteeggt 180
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cctacgcagg tacagccgcc gcttccagac cattgacatc gagcctgaca tcgaagccct 300
getgteteaa gggeteaget gtgeetaggg egeceeteet acceeggetg ettggeagtt 360
gcagtgctgc tgtctcgggg gggttttcat ctatgagggt gtttcctcta aacctacgag 420
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<212> DNA
<213> Homo sapiens
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<223> n = A, T, C or G
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<210> 472

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<212> DNA
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<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A, T, C or G
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catgcagtgc ttcagcttca ttaagaccat gatgatcctc ttcaatttgc tcatctttct 180
gngtggcgca gccctgttgg cagcgggcat ctgggtgnca atcgatgggg catcctttct 240
gaagatette gggccaetgt cgtccaetge catgcagttt gtcaacgngg getactteet 300
categeagee ggegttgtgg tntttgetet tggttteetg ggetgetatg gtgetaanae 360
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<210> 474
<211> 155
<212> DNA
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<211> 282
<212> DNA
<213> Homo sapiens
<400> 475
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tcaaaagcca aaaaatggga gacaatttca catggacttt ggaaaatatt tttttccttt 180
gcattcatct ctcaaactta gtttttatct ttgaccaacc gaacatgacc aaaaaccaaa 240
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agtgcattca accttaccaa aaaaaaaaa aaagggcggc cg
<210> 476
<211> 434
<212> DNA
<213> Homo sapiens
<400> 476
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geagtetteg aggggegtga geaegteete eaeggteegg eagegeagea egeeettget 300
gagategetg taggggtege egeegeege egeeagetee ageaceeget eeegeageeg 360
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caggacggcc aggc
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tgtacgagat ccctggactg gagcccatca cctttgcggg gaagatgcac ttcgtgccct 180
ggctggcgcg gccgatcttt ccgccctggg accgcggcta caaggaccca aggttctacc 240
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<212> DNA
<213> Homo sapiens
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acaattgagg acttctggcg aatgatctgg gagtggaaat cctgctctat cgtgatgcta 180
acagaactgg aggagagagg ccaggagaag tgtgcccagt actggccatc tgatggactg 240
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<213> Homo sapiens
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<211> 207
<212> DNA
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gcaccaccac gaggcgattt gtgggccata ccaaggatgt gctgagtgtg gccttctcct 180
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agtgcacgga agtcacaact ggtctatcag tccagacggg ggcctttggt caaatattct 180
tctgattact tccaagcccc ctctgactac agatactacc cctaccagtg cttccaaact 240
gcacaacacc cnagettnet ettecagnac aagagggtgt cetggteeet ggeetacete 300
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cccqqqcccq ctcctcaaca qtcaccqagc tgcggcggga gcagccccct tcagagctgc 180
ccggcccagc actgggccct gccagggaca cnatatccga gctggcccgt gcc
<210> 484
<211> 194
<212> DNA
<213> Homo sapiens
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gatagatagc atgtaagggg gtggttgtcc caggaggcag ctgctgacag gtttgctaca 120
cacagococg gactgtgttg cotgggtgct cattcagaga ggggctatca totgggagcc 180
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tgtgcccctg ggtc
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<211> 67
<212> DNA
<213> Homo sapiens
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<213> Homo sapiens
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       <211> 257
       <212> DNA
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                                                                        120
                                                                        180
 tttcaccgct acacgaccgg gggtatacta cggtcaatgc tctgaaatct gtggagcaaa
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 ccacagtttc atgcccatcg tcctagaatt aattccccta aaaatctttg aaatagggcc
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 cgtatttacc ctatagt
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       <211> 378
       <212> DNA
       <213> Homo sapien
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                                                                        120
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ccaggactcc tgttttggcc aggcagctca gcaataggag cagccgcatg cttctggaag
                                                                        240
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aqtatcttgg cagagcaatc tgccgcacaa actgcaaatt aaattaacta cacagactaa
                                                                        120
                                                                        180
aaactataca qcctaccatc aacagttqtq cattataaaa aggtagtttc tttccttttg
ttttaagtca ggaacaggta gatttttaaa aatatatata caagctaaca cacacrgcta
                                                                        240
tcagcactaa tgccccccc tcaacttttc ctttttctta tagaaaatgg aaagcttaca
                                                                        300
                                                                        360
ataceteste srtymwrgmr scagreetwe gageewgeet grasagggtk wgcmktggar
magmtstgkc ctgaggttta gagccgcttt gtgcggggat ggtggaggct agggtggggg
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137

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                                                                      180
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ggacaagaag gctgctggag ccggcaaggt caccaagtct gcccagaaag ctcagaaggc
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aacaatgcat cqtaaaacct tcagaaggaa aggagaatgt tttgtggacc actttggttt
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tcaataaatc agttaactta aaaaatatat tgtgaccatt tttataaaat acatgttcat
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aaaacagatc aacatattta gcttatacag aaataaaatt aagtcaatcc actcacaaag
                                                                       300
                                                                       360
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cctgcccggg cggcaagtgt gctggaattc tgcakatatc catcacactg gcggscgctc
                                                                       420
                                                                       480
qaqcatqcat ctaqaqqqcc caattsqccc tataqcqqcg cattaagcqc ggcgggkgtg
gtggwtacgc gcasygtgac cgmtacactt gccarcgccc tagmgcmcgc tcctttcgcw
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tgataatgag attgatctgt cccatggaga gtgaaagttc agttccactt ctgcctcctt
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                                                                       240
ctttccatgc tgtcctcatg ctctttatcc tcacttcctc agtcccttca acactcaaaa
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ttttcttcac aaacctctat aaaacatcag cagagaacat ataaatacat tttgattagc
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                                                                       180
qqcttqaqat ttqttqqtct tttaaaaaca araaatgggg aaatgcaaca aaatgacctt
                                                                       240
tccacttttc aaaagctttc aagtaaagga tagatcatag ggccataaaa gatccattta
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318
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                                                                        120
actttgggag gecgagecag gtggatcacg aggteaggag atcgagaeca geetggetaa
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                                                                       240
catggtgaaa ccctqtctct actaaaaata caaaaatgag ccgggcatgg tggggggca
ccgtagtccc agctacttga gaggctgaga caggagaatg gcgtgaaccc ggggggcgga
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      <221> misc feature
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                                                                       180
gtttggttag tgactgatqt aaaacggttt tcttgtgggg aggttacaga ggctgacttc
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agagtqqact tqtqtttttt ctttttaaaq aggcaaggtt gggctggtgc tcacagctgt
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tactaaaaat aaagaaatca gccatgaaa
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                                                                       180
agttttcaat qctctccagg tgtttctaaa gtgcagacaa gtttangacc gtgcttgagg
                                                                       240
qtgaaqqqca qqactqtgat ggggagggc aaatatgggg cccttggggt gcaggcaatg
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ttttcatggy ccctgakcaa ttttaaacag ttggaacacc ggtggcactg ataactgcty
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ttatatette atteaateat ttatteacaa ttagtetaat tgcattettg atgaataaet
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gacttcagca aaggagtcaa tccactaagc aaagttcatt tatttttcat qatgttcttc
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tagctctcat aatacaatat ccataatggc tttagaagaa tgtaaataaa taacattggt
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aaacagcgta tactgatatt ttctgacaaa ctcatttatc taacatcatg ctgagcaatc
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aagaggattc ctctatatat tttaaatttt aatttattct atttcctgat tcacaaactc
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ttgctccatg ttaaagcagt tatcaccaat agaacctatg agaaccagtg cccatggaaa
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actcgccggg ctggcaacct taaacaggac ggaggtgaca acatcttttg cgggtctttg accacttccc ctggaattgg gtggggctgg gatcaggtct gggctaggcc cagccacagg	ttgtagctct tcttctctga ttgtcctgga gaggtggagt	tgtcttcttt gaattgcatt agttctgctg cctgggcctg	cagctcatag ccctgccagg cagagggacc ggcatgcaga	atggtggcat cctaccacat ttgctcagag	180 240 300 360 420 461
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ccactacttt gatacggcaa ttgtgaattc cgatcttgat aaagcctatc aggaattgct
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ctaatttcta qqaaacattt attqtttata tqcaqatcct aqaqacttct atttcagtgc
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agetettttq qaageeattt ttatgttata tgtttacaag eeccacacca ggetgaaaat
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tgttgtagga agattatctg gatacacctt tgttttacac ccttctaacc taacatctgg
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taaagatctg ttgagtgcaa tcatctcact tgccattaaa ttgaactgat tgattttaaa
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catctctttc atctttctt gatcctcttt aggaatgacg actggtttcc ccatttctcc
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tcagccttgc aatttcagca tcctqcaqct tcqaqccaat qqtqaqctcc ttctqqatca
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360
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taactccagt attgccccct ctcactttag catatattaa ttagcaggtt gggctagaga
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aatcagctgc tatgcgggtt gattattatt attatttcta atccttttcc ttatttgcct
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tctactcccc ttaatctaat ctaaaagctc tgttccatgc aactggagtt ccttatccct
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aaccacaqtc aaatataatg acaacattgg atggatagat cagtaccatt ggttacagct
gttaaacagg ttcgttcttg gcgccacata aaaacaagcc aataacatcg aataaatcat
                                                                       240
qqcttttttt ttctttatca caattcactt aagtgatgtt aattatggtc cttgtcaaac
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                                                                       360
acqtttqqta aaqqctattt acaqtqtaca tqqctqaqca tqcactattt ataqttacaa
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                                                                       120
                                                                     · 180
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tcacccannc gtggatcgtt ggcattgtgg gaaaagggaa accgnaacgg cccggatcat
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cctgacagtt caaatgcctc ctttgagcct agctcgtgag atgaaagaac agaagttgtt
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tggaccttag agccattatc cacaatcacg gatggttctc aagagttgat tgtaagaaat
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tectecaete caeatgetgg ceaagggeae agagetgeeg tategeetge caagggggtg
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                                                                       240
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tcaggcgccg gtcctttgag ctttcttgat ttcctcagag agcgcctcct tcagctctgc
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                                                                       360
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gttgc
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gtctgtcatt cagtacaagg tatatttatg ttatttccaa agccatcacc ctaaaatcct
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                                                                       240
aagttgccac tcttaaaacc taaaaataat gtcgaaaact aaagtcataa atacatgtat
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ggggg
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ggaacngggg ggggcactgg gcaggaggga atgnggangn gg
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ataaaanaac natggcaact ttgncctgan tgncnccctn cccaanctga nctggntgga
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anaagaaact tggaaactat ntnanccatg gntttgggan nctnccccct tncccatgnc
                                                                    240
tnctaataaa accatgcant gcctttggag agaagagacc ccc
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tttctttttc atgatgnggn acctccnaag ngatggnaga tttaaataat tttttatttt
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tattttatat atttnttcat tagggccttt tctcccnaaa acgaaanaaa aantccnaaa
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aacnaaaccc aaaaaaanag agggtantgt ccnagtttct gtatgtataa agtcntncnc
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                                                                       120
ctcttaacat ttctttatca gacgccactg gcttcctaaa atggaccctg gactatgtat
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ggggaccaca ttcattatgc tgcctttcct cttatgatta aaactttagc cctcattcga
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nggttccaat ggtactttta gnggaggagt ccctagcttt taaaaaaacc acttttcctn
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taaaatccnt tntttatnga aaaaaancnt ttttaaaaat gttaaggagg attttaaatg
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      <211> 415
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tegteatteg aaacatagtg gaggeegeag cagteaggga catttetgaa gegagegtet
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tcgatgccta tgtgcttccc aagctgtatg tgaagctaca ttactgtgtg agttgtgcaa
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ttcacagcaa agtagtcagg aatcgatctc gtgaagcccq caaggaccqa acacccccac
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cccgatttag acctgcgggt gctgccccac gtcccccacc aaagcccatg taaggagctg
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gacctctaac tcattgaagc aggacacctg aacttgttgg acatacttgg gcaagatttc
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agccacatac tetecaaaag etgagagetg ettgtgggee acateattee gtggtetgae
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agtggggggg gtgtcggccc cggcgctctc ccqcctcacc qqcaqcaaca qaacqqagqq
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tegeceagte eccetggtea gegeegagge ecceaagate eegegeeace acageetgge
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gctttcctca tcatcagaat tcaaactttg ggcaaacatg ggttttgggc tgantctttg
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gaatatgctg gaaaaacccc aatatgggct gcttctgctt gtttggcatg acgcaaaatg
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gnttcccang atactgcatc gtcttgccaa gaatgttcca ttagaaaaag gcccgggtcc
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tegecacact ggetggeete tgetgggtge ntetagagta tateggetge aceteagtge
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atagagetgg aaactgcagg tgttataccc aacctattca tectcaacac tgtagtcacq
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ccccggaaac tactcagggc accaaacatc caaaacataa actattatta tacaaagaaa
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aacaatggca cttgggctct tgcttaatct agattgtctt caaaaagtct ctaaaatgng
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ggacagggcg tecacatgte gttgtgggte tggctggatt ttgaggtgcc gaggaactgg
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acaataattc aagtagagtg tcccagaaaa aaaccacttg ggctccctgt ttggagtctg
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gctggctctg agcattgcca atggccccta ctcacctgac tttgtatcct ctccttttaq
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tgtttcattt gggagttatt tggccagggc cttttgaaca gtaagtgtcc ccatgaagtg
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240
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catactggaa attgcctaac ttaatcattg cctaaagaag agaaaattat ccccaaaacg
                                                                       180
tgcttaacca ggaggccaat gcatttgccg acctccaaga acatggagat gaacgtgata
                                                                       240
gacagactgt ccaccatctg aaccttcatt caccaccatt cgataaccct tattcaggcc
cagatcagca gcacatttct tgccaacaat cattaagtgt ccaagaagac tttcatcatc
                                                                       300
                                                                       360
atcttctgcc acagaaatct gggatatatg tttcttgggt atcaccagaa aatgtgttgg
                                                                       420
tgcttgaggg gaaatgtcat ggaaagcaag gcaccggtca tccttaaaaa tgattttggc
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      <211> 158
      <212> DNA
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      <221> misc_feature
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aaaggnccct ttccgggacc ggnccnggac ccacctttgg gcccaaaggg ggatttaccg
                                                                       120
                                                                       158
ggtaaaccaa gcctttaaag cgttgggggt taaatttc
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      <211> 159
      <212> DNA
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      <222> (1)...(159)
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gcagccgacc atctttcaaa acaagaagag ggtcctgctg ggagaaactg gcaaggagaa
                                                                       120
                                                                       159
gctcccgcgg tnctacaaga acatcgntct gngnttcaa
      <210> 612
      <211> 419
      <212> DNA
      <213> Homo sapien
      <400> 612
gcatttttta ttaagacatt tggggcccga gtttcctctc ctcctcccct ccatcctgtg
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ctctctaaat tcagcttttg gaaacctaag tgtgcccacc ttccccagca ggtagccaga
                                                                       120
gcctccgggg tccctcttcc ttccttcttt ctccccagat actgcaagag acacccaagt
                                                                       180
```

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ctgctgtcag cagagggtga agcgtctggc actgatgttc atgcgcgtga gtcccagatg
                                                                        240
ccgcagcggt ggggccagag gcaagccagt cccagactct aactccatct ccagctcagc
                                                                        300
ctcatccaga agctcctggt gcaggtgaca gacttggtcc actttcagtc tgtgcagccg
                                                                        360
ggcccgcagc ctgagcagct gccctgccag ctgccggtcc tgagcccgca tctcctgca
                                                                        419
      <210> 613
      <211> 419
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(419)
      \langle 223 \rangle n = A, T, C or G
      <400> 613
ccccatactg aggcatataa agtttgcaaa accaaggggc ctgtcttccc aaggtcttac
                                                                         60
tataaaatct gggttaggct aaaacttatt atgtagacca gagaggcgtt gattttaaac
                                                                        120
caatcatcct gtctcatctt cattatttct ggctttatga gcagaatgtc ctgctacctt
                                                                        180
tggcttctta taaagatctt taatggagta ttttaaacat tggaaaatcc atgagtttga
                                                                        240
gettatttgg agaatgetge taagaatggg attgactgae ataacttact ageetettte
                                                                        300
ctgcttgagg tacagcagtt ttcaatccca atgtgtaaag tgcttagaag ttatcactcc
                                                                        360
ccaccttaga gcaaaaacct tcagagaact tcagncactc caccaggcaa atagcacct
                                                                        419
      <210> 614
      <211> 123
     <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A, T, C or G
      <400> 614
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catgataggg aaantnatte tgaggennga ngettnaetg aattntttee anceagnggt
                                                                        120
ntt
                                                                        123
      <210> 615
      <211> 362
      <212> DNA
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      <400> 615
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accgagacca catcactatt ccatatttga gcaggccagc atcgtggaag cgcttttgcg
                                                                        120
gcatctgggg ctccagaacc gcaggatcaa ccttctttct catgactatq qagatattqt
                                                                        180
tgctcaggag cttctctaca ggtacaagca gaatcgatct ggtcggctta ccataaagag
                                                                        240
tetetgtetg teaaatggag gtatetttee tgagaeteae egteeaetee tteteeaaaa
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getactcaaa gatggaggtg tgctgtcacc catcctcaca cgactgatga acttctttgt
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at
                                                                        362
      <210> 616
      <211> 210
      <212> DNA
      <213> Homo sapien
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<220>
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cgccagcctc agccaggtgg gcctgtatat agggtccatg tgcaataggg agggacgtct
                                                                       120
tetatttttt getgeeceet eeeggeecae tgtetngggg cagggggaga aggtatttte
                                                                       180
nagataaagc acangcacca caaataaaag
                                                                       210
      <210> 617
      <211> 511
      <212> DNA
      <213> Homo sapien
      <400> 617
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                                                                        60
ggaggaaaca gtgacagacc tggagactgc agttctctat ccttcacaca gctctttcac
                                                                       120
catgcctgga tcacttcctt tgaatgcaga agcttgctgg ccaaaagatg tgggaattgt
                                                                       180
                                                                       240
tgcccttgag atctattttc cttctcaata tgttgatcaa gcagagttgg aaaaatatga
tggtgtagat gctggaaagt ataccattgg cttgggccag gccaagatgg gcttctgcac
                                                                       300
agatagagaa gatattaact ctctttqcat qactqtqqtt caqaatctta tqqaqagaaa
                                                                       360
taacctttcc tatgattgca ttgggcggct ggaagttgga acagagacaa tcatcgacaa
                                                                       420
atcaaagtct gtgaagacta atttgatgca gctgtttgaa gagtctggga atacagatat
                                                                       480
agaaggaatc gacacaacta atgcatgcta t
                                                                       511
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      <211> 511
      <212> DNA
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      <400> 618
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                                                                       120
tocagotyte coettitety gyactatica aggagytete caggacygae ticagateae
                                                                       180
tgtcaatggg accgttctca gctccagtgg aaccaggttt gctgtgaact ttcagactgg
cttcagtgga aatgacattg ccttccactt caaccctcgg tttgaagatg gagggtacgt
                                                                       240
ggtgtgcaac acgaggcaga acggaaqctq qgqqcccgag gagaggaaga cacacatgcc
                                                                       300
tttccagaag gggatgccct ttgacctctg cttcctggtg cagagctcag atttcaaggt
                                                                       360
gatggtgaac gggatcctct tcgtgcagta cttccaccgc gtgcccttcc accgtgtgga
                                                                       420
caccatetee gteaatgget etgtgeaget gteetacate agetteeage etceeggegt
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cacgggcagc attgctggag ccccagagga tgaaagatcg cagagcacag cccccaggc
accagagtgc ttcgaccctg ccggaccggc tgggctcgtg aggccgacat ctggcctttc
                                                                       180
ccagggccca ggaaaggaaa ccttggaaag tgctctaatc gctctagact ctgaaaaacc
                                                                       240
caagaaactt cgcttccacc caaagcagct gtacttctct gccaggcagg gtgagctgca
                                                                       300
gaaggtgctt ctcatgctgg ttgatggaat tgatcccaac ttcaaaatgg agcaccaaag
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taagcgttcc ccattacatg ctgctgcgga ggctqqccac gtggacatct gcc
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<210> 620
      <211> 415
      <212> DNA
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gtgttggtat taggagatet geacateeca caeeggtgea acagtttgee agetaaatte
                                                                        120
aaaaaactcc tggtgccagg aaaaattcag cacattctct gcacaggaaa cctttgcacc
                                                                        180
aaagagagtt atgactatct caagactctg gctggtgatg ttcatattgt gagaggagac
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ttcgatgaga atctgaatta tccagaacag aaagttgtga ctgttggaca gttcaaaatt
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ggtctgatcc atggacatca agttattcca tggggagata tggccagctt agccctgttg
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cagaggcaat ttgatgtgga cattcttatc tcgggacaca cacacaaatt tgaag
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      <210> 621
      <211> 421
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A, T, C or G
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gaaagacttc agatggaaca gaaataaatg ccttttttga caaacgcagc agtgcgtqcc
                                                                        120
tctagcttgc aagagcgtta ctccccttca tagctttaaa aggttttcgc actgcgtgca
                                                                        180
gttagagtag ctaaatcttg tqtgacqctc cacaaacact tqtaagaatt ttgcagagaa
                                                                        240
agataaccgt tgccacccaa tgccccccac aggcattcta ctccccagta cctcttaggg
                                                                        300
tgggagaaat ggtgaagagt tgttcctaca acttgctaac ctagtggaca gggtagtaga
                                                                        360
ttagcatcat ccggatagat gtgaagagga cggctgtttg gataataatt aaggataaaa
                                                                        420
                                                                        421
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      <211> 431
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(431)
      <223> n = A, T, C or G
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aaaaagagaa tgcagtaact aatgccctaa atgtttgatc tctgtttgtc attacttttt
                                                                      . 120
caaaattatt tttttctgta aagtataata tataaaactt cttgcttaaa ttgaatttct
                                                                       180
atattagtgg ttaattgcag tttattaaag ggatcattat cagtaatttc atagcaactg
                                                                       240
ttctagtgtt ttgtgttttt aaaacagaat taggaatttg agatatctga ttatattttt
                                                                       300
catatgaatc acagacctcg gccgcgacca cgctaagggc gaattccagc acactggcgg
                                                                       360
ccgctactag tggatccgag ctcggtacca agcttgggcg taatcatggt cataqcctqt
                                                                       420
ttcctgtgtg a
                                                                        431
      <210> 623
      <211> 421
     <212> DNA
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<220>
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      <222> (1)...(421)
      <223> n = A, T, C or G
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                                                                       120
aatcttccca ttcccagaat ccagaatttt qqaaqccatt ttaaccaggg gtattttttn
                                                                       180
                                                                       240
caccattacc ttttqqaact ttccaaatta atggcctttt aaaaaggttg gaaggggaaa
                                                                       300
accaaaaggc caaaatttta aaaaggttgg ggggggaac cttaaaaaaa aaaatgggtt
                                                                       360
ttggggccnc ctttttttaa aaggccaaaa nttttttggg ttccaattaa aaaaatttcc
                                                                       420
tttttccaac ccaaaattaa gaaaaggnaa aattaaaaaa attncaaaaa ttggnttttt
                                                                       421
      <210> 624
      <211> 421
      <212> DNA
      <213> Homo sapien
      <400> 624
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ccactccaag tcacacccg agaccaagcc ccacaagtgc ccacattgct ccaagacctt
                                                                       120
cgccaacagc tcctacctgg cccagcacat ccgtatacac tcaggggcta agccctacag
                                                                       180
                                                                       240
ttqtaacttc tqtqaqaaat ccttccqcca qctctcccac cttcaqcaqc acacccgaat
                                                                       300
ccacactggt gatagaccat acaaatgtgc acacccaggc tgtgagaaag ccttcacaca
actotecaat etgeagtece acagaeggea acacaacaaa gataaaccet teaagtgeea
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caactgtcat cgggcgtaca cggatgcagc ctcactagag gtgcacctgt ctacgcacac
                                                                       420
                                                                       421
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      <211> 421
      <212> DNA
      <213> Homo sapien
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ggggccaggc aagagttagc catgaagagc ctcaagtccc gcctgaggag gcaggacgtg
                                                                       120
cccggccccg cgtcgtctgg cgccgccgcc gccagcgcgc atgcagcaga ttggaataaa
                                                                       180
                                                                       240
tatgatgacc gattgatgaa agcagcagaa aggggggatg tagaaaaagt gacgtcaatc
cttgctaaaa agggggtcaa tccaggcaaa ctagatgtgg aaggcagatc tgtcttccat
                                                                       300
gttgtgacct caaaggggaa tcttgagtgt ttgaatgcca tccttataca tggagttgat
                                                                       360
attacaacca gtgacactgc agggagaaat gctcttcacc tggctgctaa gtatggacat
                                                                       420
                                                                       421
g
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      <211> 476
      <212> DNA
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catagacaat agacatagcc aaaacttatt ctaaaataca tatgaagatg cacaggccct
                                                                       120
aqttatacaa tcttgacaaa gaagaataaa gtgggaagaa tctatttgat tttaaggctt
                                                                       180
                                                                       240
accatgtaac tacagtcatc aagagagtgt ggtatcggca gacggtcaga catacagatc
aatqqaatqt aacaqaqqac ccaqaaataq qcccacacaq atatqctcaa tqqatatttq
                                                                       300
                                                                       360
acaagcgtgc aaaacaattc aatggaagaa taagctttca aaaaaatggc gttggagcaa
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ccggacatcc ataggaaaaa acacaaaatg aatcataggc					420 476
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<210> 628 <211> 248 <212> DNA <213> Homo sapi	en				
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atcatgtttg tagacccttc					420
agattgtaca catatgagcc ttaagactta ttcagtcaga					480 540
gtcaaatttc atgaagaaaa gattttgtaa tattactatt	cctctggcac	attgacaaat	actaaatgtg	caagtatata	600 640

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     <212> PRT
     <213> Homo sapien
     <400> 631
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1
                5
                                   10
Thr Val Ser Ser Asn Leu Ala Ile Ala Ile Lys Lys Glu Lys Arg Pro
Pro Gln Thr Leu Ser Arg Gly Trp Gly Asp Asp Ile Thr Trp Val Gln
                           40
Thr Tyr Glu Glu Gly Leu Phe Tyr Ala Gln Lys Ser Lys Lys Pro Leu
                       55
Met Val Ile His His Leu Glu Asp Cys Gln Tyr Ser Gln Ala Leu Lys
                                       75
                   70
Lys Val Phe Ala Gln Asn Glu Glu Ile Gln Glu Met Ala Gln Asn Lys
                                   90
Phe Ile Met Leu Asn Leu Met His Glu Thr Thr Asp Lys Asn Leu Ser
                               105
Pro Asp Gly Gln Tyr Val Pro Arg Ile Met Phe Val Asp Pro Ser Leu
                                               125
                           120
Thr Val Arg Ala Asp Ile Ala Gly Arg Tyr Ser Asn Arg Leu Tyr Thr
                       135
                                           140
Tyr Glu Pro Arg Asp Leu Pro Leu Leu Ile Glu Asn Met Lys Lys Ala
                   150
                                       155
Leu Arg Leu Ile Gln Ser Glu Leu
               165
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     <221> misc feature
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gctttacctc gctgacccta tgaaggcacg tgtggttctc aaatataggc attctgatgg
                                                                     180
gaacttgtgt gttaaagtaa cagatgattt agtttgtttg gtgtataaaa cagaccaagc
                                                                     240
tcaagatgta aagaaaattg agaaattcca cagtcaacta atgcnactta tggtacccaa
                                                                     300
360
tacttaggaa gtaaatatct tttgaattan aaaaagtgtt gg
                                                                     402
      <210> 633
      <211> 402
      <212> DNA
      <213> Homo sapien
      <220>
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      <222> (1)...(402)
      <223> n = A, T, C \text{ or } G
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<211> 386 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)(386) <223> n = A,T,C or G	
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<210> 635 <211> 404 <212> DNA <213> Homo sapien	
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<210> 636 <211> 403 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(403) <223> n = A,T,C or G	
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300
cagatggctc cccagccctg aaacaqatcg aaatcaacac catctctgcc agctttgggg
gcctggcctc ccggacccca nctgtgcacc gacatgttct cagtgtcctg agtaagacca
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aagaagctgg caagatcctc tctaataatc ccagcaaggg act
                                                                       403
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      <211> 441
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      <221> misc_feature
      <222> (1)...(441)
      <223> n = A, T, C or G
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tagaagggat gacccaaagt ctgaaggtc tggaattaga tgttgttact ataaggtcag
                                                                       120
aaaaagaaaa totgacaaat gaattacaaa aagagcaaga gogaatatot gaattagaaa
                                                                       180
taataaatto atcatttgaa aatattttgo aagaaaaaga gcaagagaaa gtacagatga
                                                                       240
aagaaaaatc aagcactgcc atggagatgc ttcaaacaca attaaaagag ctcaatgaga
                                                                       300
gagtggcagc cctgcataat gaccaagaag cctgtaaggc caaagagcag aatcttagta
                                                                       360
gtcaagtaga gtgtcttgaa cttgagaagg ctcagttgct acaaggcctt gatgaggcca
                                                                       420
aaaataatta tattgtttgc a
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      <211> 404
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      <220>
      <221> misc feature
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      <223> n = A, T, C or G
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tecegattee tittggttee aagteeaata tggeaactet aaaggateag etgatitata
                                                                       120
atcttctaaa ggaagaacaq accccccaga ataaqattac aqttqttqqq qttqqtqctq
                                                                       180
ttggcatggc ctgtgccatc aqtatcttaa tgaaggactt ggcagatgaa cttgctcttg
                                                                       240
ttgatgtcat cgaagacaaa ttgaagggag agatgatgga tctccaacat ggcagccttt
                                                                       300
tcttagaaca ccaaagattg tctntqqcaa agactataat qtaactqcaa ctncaqctqq
                                                                       360
cattatcacg ntggggacgt cagaagaagg agaaagccgc ttat
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      <210> 639
      <211> 404
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A, T, C or G
      <400> 639
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cagcettage tteggetece ggettqqqtq qeqeqqeeqt qeeetegttt tqqcetecqa
                                                                       120
acgcggctcg aatggcaagc caaaattcct tecggataga atatgatacc tttggtgaac
                                                                       180
taaaggtgcc aaatgataag tattatggcg cccagaccgt gagatctacg atgaacttta
                                                                       240
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agattggagg tgtgacagaa cgcatgccaa ccccagttat taaaqctttt ggcatcttga
                                                                       300
aacgagcggc cgctgaagta aaccaggatt atggtcttga tccaaaaatt gctaatgcaa
                                                                       360
taatgaangc agcanatgaa gnanctgaag gtaaataaaa tgat
                                                                       404
      <210> 640
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 640
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                                                                       120
agaggcctcc tcagacactc tcaagaggat ggggagatga catcacttgg gtacaaactt
                                                                       180
atgaagaagg totottttat gotcaaaaaa qtaagaagco attaatggtt attoatcaco
                                                                       240
tggaggattg tcaatactct caagcactaa aqaaagtatt tgcccaaaat qaagaaatac
                                                                       300
aagaaatggc tcagaataag ttcatcatgc taaaccttat gcatgaaacc actgataaga
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atttatcacc tgatgggcaa tatgtgccta gaatcatgtt t
                                                                       401
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      <211> 404
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(404)
      <223> n = A, T, C or G
      <400> 641
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                                                                       120
gattcgagca gaaggggttc cgctggtggc catgaagttc cttcgggctn ttgaagaaca
                                                                       180
cctgaacagc attacatcga ccctgaacga accgtccttt ctttccnqqq qctqqtqaaa
                                                                       240
tacatgaact tnggggccat ngtgggcatg ggcttgggaa ggggntcaat ggtggtggaa
                                                                       300
aaccggcccg aatgattctt ggggggaana acaaatccaa nttgatttaa aaaccaggca
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nccattnccg ggggggattt tnttgnnttt naaanttggg nagg
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      <211> 366
      <212> DNA
      <213> Homo sapien
      <220>
    <221> misc feature
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      <223> n = A, T, C or G
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                                                                       120
cagcagcatg ggggtaacgg coccatgatt caattacctc ccactgagtc cctcccacqa
                                                                       180
catatgggga ttatgggagc tacaattcaa gatgagattt aggtggggac acagccaaac
                                                                       240
catttcaata gcataacacc aaaaaaggtt atagagcagt aaaagggttq atggaccatq
                                                                       300
catcagtaat aataataata attataagtg atctttaaac attcatcagg tgccaagcct
                                                                       360
cgtgcc
                                                                       366
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<210> 643 <211> 403

180

240

300

360 403

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      <221> misc feature
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ccaggaatcc acaatgatgc agganaagat gaagaaccaa gacccaactt tnancaacct
aaaaannntt ccnagggnn ttnanngttt nanggncntt ntccccaant tttnagganc
cattgttnat ngntgnncaa aannagttng gnggaaatcc ttttgtttcc ttgggganca
atacatcctt tggngaaggt agtcaacctt cccgtncana aattagaaat cccctnccca
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      <211> 403
      <212> DNA
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<213> Homo sapien <220>

<221> misc feature <222> (1)...(403) <223> n = A, T, C or G

<400> 644

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<210> 645 <211> 405 <212> DNA <213> Homo sapien <220> <221> misc feature

<222> (1)...(405) $\langle 223 \rangle$ n = A, T, C or G

<400> 645

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<210> 646 <211> 412

<212> DNA

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<213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(412)
      <223> n = A, T, C or G
      <400> 646
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aaaccggcct tgtggaattt gcaagaaacc tgaccgctct tggtttgaat ctggtcgctt
                                                                       120
ccggagggac tgcaaaagct ctcagggatg ctggtctggc agtcagagat gtctctgagt
                                                                       180
tgacgggatt tcctgaaatg ttggggggac gtgtgaaaac tttgcatcct gcagtccatg
                                                                       240
ctggaatcct agctcgtaat attccagaag ataatgctga catggccaga cttgatttca
                                                                       300
atcttataag agttgttgcc tgcaatctct atccctttgt aaagacaagt ggcttctcca
                                                                       360
ggtgtaactg ttgaggangc tgtgggagca aattgacatt ggtgggagta ac
                                                                       412
      <210> 647
      <211> 412
      <212> DNA
      <213> Homo sapien
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      <221> misc feature
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      <223> n = A, T, C or G
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                                                                       120
                                                                       180
tgaacaaaaa agttanntag ctaaaacagg acttgcagnn ttnaaaacag gtccttgatg
gcaaagaaga ggttgagaaa caacntagag aaaatattna aantctaaat tccatggtag
                                                                       240
aacqccaaga gaaagatctt ggccgtcttc aggtagacat ggatgaactt gaagaaaaga
                                                                       300
accgaagtat tcangctgcc tggatagtgc atacaaagaa cttactgatc tttacaaagc
                                                                       360
caatgctqca aanqataqtg aqqnacanga agctqctctn accqtgaaat ga
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      <211> 413
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A, T, C or G
      <400> 648
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                                                                        60
cggctctgcc cggctgccgc ccggcatgaa catcatggat ttcaacgtga agaaacttgg
                                                                       120
cgggccgacc gggcaccttt tcttaagccg gcccgtgnaa tttanaaaaa aaaaacttgg
                                                                       180
ncaagcaaaa aaaaanaaaa ttggncctta ncttgaaaan cttcttaaca aaacttaatg
                                                                       240
gtccaaaata ttgaccgaaa aaaaaatgna ncaaaccnna ntgnttttgc acccaatncn
                                                                       300
aatnoonnga nnaaaaaaat tgnttattaa aaacntgaat aaaaancccc aannotatna
                                                                       360
acaaccccga actttttgga cnatntntna ntgatnnnng aacntaattt ggc
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      <210> 649
      <211> 409
      <212> DNA
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<213> Homo sapien

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      <223> n = A, T, C or G
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cacccccgcq gtcctcggga ggctagagat catggaaggg aagtggttgc tgtgtatgtt
                                                                        180
actggtgctt ggaactgcta ttgttgaggc tcatgatgga catgatgatg atgtgattga
                                                                        240
tattgaggat gaccttgacg atgtcattga agaggtagaa gactcaaaac cagataccac
                                                                        300
tgctcctcct tcatctccca aggttactta caaagctcca nttccaacag gggaagtata
ttttgctgat tcttttgaca gaggaactct gtcagggtgg attttatnca nagccaanaa
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                                                                        409
      <210> 650
      <211> 413
      <212> DNA
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      <220>
      <221> misc feature
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gacgtgggct ttaccatgag taactccatt cctggtatag aatccccatt tgaacaagca
                                                                        120
aagaaggtga taaccatgtt tgtacagcga caggtgtttg ctgagaacaa ggatgagatt
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gctttagtcc tgtttggtac agatggcact gacaatcccc tttctggtgg ggatcagtat
                                                                        240
                                                                        300
cagaacatca cagtgcacag acatctgatg ctaccagatt ttgatttgct ggaggacatt
gaaagcaaaa tccaaccagg ttctcaacag gctgacttcc tggatgcact aatcgtgagc
                                                                        360
atggatgtga ttcacatgaa acaataggaa agaagtttga gaanaagcat att
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      <210> 651
      <211> 441
      <212> DNA
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      <220>
      <221> misc feature
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tcacctggct gctaagtatg gacatgcatt gtgcctacaa aaacttctac agtacaattg
                                                                        120
teceaetgag eatgeagace tgeagggaag aactgeaett eaegatgeeg eaatggeaga
                                                                        180
ttgtccttct agcatacagc tgctttgtga ccatggggcc tctgtgaatg ccaaagatgt
                                                                        240
                                                                        300
agacgggegg acaccacttg ttctggctac tcagatgagt aggccaacaa tgtgtcaact
                                                                        360
gctgatagat agaggagcgg atgttaattc cagagacaaa caaaacagaa ctgccctcat
                                                                        420
gctaggttgc gaatatggtt gcagagatgc agtagaagtc ttaattaaaa atgggtgctg
                                                                        441
atataagett getggatgeg e
      <210> 652
      <211> 412
      <212> DNA
      <213> Homo sapien
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<210> 654 <211> 404 <212> DNA <213> Homo sapi	.en	,	·		
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<210> 655 <211> 402 <212> DNA <213> Homo sapi	en				,
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<212> DNA

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<213> Homo sapien

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                                                                       120
                                                                       180
tgacaccatc gagaatgtca aggcaaagat ccaagataag gaaggcatcc ctcctgacca
gcagaggctg atctttgctg gaaaacagct ggaagatggg cgcaccctgt ctgactacaa
                                                                       240
catccagaaa gagtccaccc tgcacctggt gctccgtctc agaggtggga tgcaaatctt
                                                                       300
cgtgaagaca ctcactggca agaccatcac ccttgaggtc gagcccagtg acaccatcga
                                                                       360
gaacgtcaaa gcaaagatcc aggacaagga aggcattcct cctgaccagc ag
                                                                       412
      <210> 661
      <211> 411
      <212> DNA
      <213> Homo sapien
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ggaggaacag cagcgactga tcaacgacct gacaacccag agaggacgac tgcagaccga
                                                                       180
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                                                                       240
gggcaaacag gcattcactc aacagattga ggagctaaag aggcaacttg aagaggaagt
                                                                       300
aaaggccaag aacgcgctgg cccacgccct gcagtcctcc cgccatgact gtgacctgct
                                                                       360
gcgggaacag tacgaggagg agcaggagtc taaggctgaa ctgcagaggg c
                                                                       411
      <210> 662
      <211> 414
      <212> DNA
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                                                                        60
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                                                                       120
gctcaacgtg ggaatgtctg tttacatcca aggagtggcc agcgagcaca tgaagcggtt
                                                                       180
                                                                       240
cttcgtgaac tttgtggttg ggcaggatcc gggctcagac gtcgccttcc acttcaatcc
geggtttgac ggctgggaca aggtggtctt caacacgttg cagggcggga agtgggcag
                                                                       300
cgaggagagg aagaggagca tgcccttcaa aaagggtgcc gcctttgagc tggtcttcat
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agtcctggct gagcactaca aggtggtggt aaatggaaat cccttctatg agta
                                                                       414
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      <211> 414
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
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      <223> n = A, T, C or G
      <400> 663
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                                                                        60
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                                                                       120
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agcggatgtt caatggtgan aagatcaact acaccegang gtcgagccgt gctgcacgtg
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ttgncctnnn ataatttnaa ttggngagga gaanntnttn tnatcaaaag ttnttttana
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                                                                        240
aaaagntann ncatcttnnn ntaatnaaag tattacanna ntnactgccn attgacttta
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nanaaaannt aanttnnntn ganntaatet ttgnttgeag ettateatnn ttngntatna
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gatggaactt gaagtggcag agagaaaatt atccttccat aatctgcagg aagaaatgca
                                                                        180
                                                                        240
tcatctttta gaacagtttg agcaagcagg ccaagcccag gctgaactag agtctcggta
tagtgctttg gagcagaagc acaaagcaga aatggaagag aagacctctc atattttgag
                                                                        300
tcttcaaaag actggacaag agctgcagtc tgcctgtgat gctctaaagg atcaaaattc
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                                                                       120
ctggaaggca ctcattgaga tggagaagca gcancaggac caagtggacc gcaacatcaa
                                                                       180
                                                                       240
qqaqqctcqt qaqaaqctqq aqatqqaqat qqaaqctqca cqccatqaqc accaqqtcat
qctaatqaqa caqqatttqa tqaqqcqcca aqaaqaactt cqqaqqatqq aaqaqctqca
                                                                       300
caaccaagag gtgcaaaaac gaaagcaact ggagctcagg caggaggaag ancgcaggcg
                                                                       360
ccgtgaagaa ganatgcggc ggcagcaaga agaaatgatg cggcgacagc a
                                                                       411
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      <211> 411
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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cattcatata agaatccagc aacggaacgg cagaaagaca ctgactactg ttcagggcat
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tgcagatgat tatgacaaaa agaaacttgt gaaagctttc aaaaagaaat ttgcctgtaa
                                                                        300
tggtactgtg attgaacatc ctgaatacgg agaggttatt cagcttcaag gtgaccaaag
                                                                       360
aaaaaacatc tgccagtttc tcttggaggt tggcattgta aaggaggaac a
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gaaaaattat aaccaagcat aatatagcaa ggactaaccc ctataccttc tgcataatga
                                                                       180
attaactaga aataactttg caaggagagc caaagctaag acccccgaaa ccagacgagc
                                                                       240
tacctaagaa cagctaaaag agcacacccg tctatgtagc aaaatagtgg gaagatttat
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aggtagaggc gacaaaccta ccgagcctgg tgatagctgg ttgtccaaga tagaatctta
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gttcaacttt aaatttgccc acagaaccct ctaaatcccc ttgtaaatt
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ggacgagggg gccgcggctt cctccgggga ccttggcttq cctqqattqc caqqaqctqq
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aagttgacat tgagtctagg ctgaggatgg aaggtgtgga gctgaaggaa gaatggcagg
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atgaagattt tccaatacct ttaccagaag atgacagcat tgaagcagat acactagatg
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gaactgatcc agacagacag cctggctcct tagaagttaa tqgqaacaaa qtaaqqaaqa
                                                                       360
aactgatggc cccagacatc agcctgaccc tggatcctgg tgaagactct ct
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      <211> 413
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(413)
      <223> n = A, T, C or G
      <400> 674
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                                                                       120
agaatcgtat tggttacagc tggtacaaag gcgaaagagt ggatggcaac agtctaattg
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taggatatgt aatàggaact caacaagcta ccccagggcc cgcatacagt ggtcgagaga caatataccc caatgcatcc ctgctgatcc agaacgtcac ccagaatgac acaggattct ataccctaca agtcataaag tcagatcttg tgaatgaaga agcaaccgga cagttccatg tatacccgga gctgcccaag ccctccatct ncagcaacaa ctccaacccc gtg	240 300 360 413
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<220> <221> misc_feature <222> (1)(411) <223> n = A,T,C or G	
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<210> 676 <211> 413 <212> DNA <213> Homo sapien	
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      <400> 678
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                                                                       120
caacataatt tottactatg tgagtgagga totgaaagga taagaaagga gacattotot
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tggatgaaaa ttgctgtgta gagtccttgc ctgacaaaga tggaaagaaa tgccttttc
                                                                       240
togtaaaatg ttttgataag acttttgaaa toagtgotto agataagaag aagaaacagg
                                                                       300
agtggattca agccattcat tctactattc atctgttgaa gctgggcagc cctccaccac
                                                                       360
acaaagaagc ccgccagcgt cggaaagaac tccggaagaa gcagctggct
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acttgtctca ctagtgccta aatgtagtaa aggctgctta agttttgtat gtagttggat
                                                                       180
tttttggagt ccgaaggtat ccatctgcag aaattgatgc ccaaattgaa tttggattca
                                                                       240
agtggattct aaatactttg cttatcttga agagagaagc ttcataagga ataaacaagt
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tgaatagaga aaacactgat tgataatagg cattttagtg ggctttttaa tgntttctgc
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                                                                       120
gtctacgggt gggtcctgga actttggccc ccaggactct aatgacaaca aatggggtga
                                                                       180
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                                                                       240
tgagttgaaa attggagaat ggagtggtcc aaaccaacca aattctagca ctggagcatg
                                                                       300
ggacaatcaa aagggccacc ccctccctga aaaccaaggc aatgcccagg ctccctgttg
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gtgaagccca atgcaaacag aattgcttta gatttccaaa gagggaatga tgttgccttc
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cactttaacc cacgcttcaa tgagaacaac aggagagtca ttgtttgcaa tacaaagctg
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                                                                                                                    120
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His Leu Glu Val Lys Al	la Ser Leu Met Asn Asp	Asp Phe Glu Lys Ile
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Trp Ala Lys Lys Leu Ly	vs Glu Val Glu Ala Ala	Lys Lys Ala His His
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Ala Ala Cys Lys Glu Gl	u Lys Leu Ala Ile Ser	Arg Glu Ala Asn Ser
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Ser	Ser	Pro	Ile	Ile 325	Ile	Gln	Leu	Leu	Ser 330	Asp	Arg	Cys	Leu	Gln 335	Val
Leu	Asn	Ara	His	Len	Thr	Val	Len	Ara	Val	Val	Gln	Len	Gln	Pro	Len

340 345 350 Gln Gln Val Asn Leu Ile Leu Ser Asn Asn Arg Gly Cys Arg Thr Leu 360 Leu Leu Lys Ile Pro Lys Glu Tyr Asp Leu Val Leu Leu Phe Ser Ser Glu Glu Glu Arg Gly Ala Phe Val Gln Gln Leu Trp Asp Phe Cys Val 390 Arg Trp Ala Leu Gly Leu His Val Ala Glu Met Ser Glu Lys Glu Leu 410 Phe Arg Lys Ala Val Thr Lys Gln Gln Arg Glu Arg Ile Leu Glu Ile 425 Phe Phe Arg His Leu Phe Ala Gln Val Leu Asp Ile Asn Gln Ala Asp Ala Gly Thr Leu Pro Leu Asp Ser Ser Gln Lys Val Arg Glu Ala Leu 455 Thr Cys Glu Leu Ser Arg Ala Glu Phe Ala Glu Ser Leu Gly Leu Lys 470 475 Pro Gln Asp Met Phe Val Glu Ser Met Phe Ser Leu Ala Asp Lys Asp 485 490 Gly Asn Gly Tyr Leu Ser Phe Arg Glu Phe Leu Asp Ile Leu Val Val 505 Phe Met Lys Gly Ser Pro Glu Asp Lys Ser Arg Leu Met Phe Thr Met Tyr Asp Leu Asp Glu Asn Gly Phe Leu Ser Lys Asp Glu Phe Phe Thr 535 Met Met Arg Ser Phe Ile Glu Ile Ser Asn Asn Cys Leu Ser Lys Ala 550 555 Gln Leu Ala Glu Val Val Glu Ser Met Phe Arg Glu Ser Gly Phe Gln 565 Asp Lys Glu Glu Leu Thr Trp Glu Asp Phe His Phe Met Leu Arg Asp His Asp Ser Glu Leu Arg Phe Thr Gln Leu Cys Val Lys Gly Gly 595 Gly Gly Gly Asn Gly Ile Arg Asp Ile Phe Lys Gln Asn Ile Ser Cys 615 Arg Val Ser Phe Ile Thr Arg Thr Pro Gly Glu Arg Ser His Pro Gln 630 635 Gly Leu Gly Pro Pro Ala Pro Glu Ala Pro Glu Leu Gly Gly Pro Gly 645 650

Leu Lys Lys Arg Phe Gly Lys Lys Ala Ala Val Pro Thr Pro Arg Leu Tyr Thr Glu Ala Leu Gln Glu Lys Met Gln Arg Gly Phe Leu Ala Gln 680 Lys Leu Gln Gln Tyr Lys Arg Phe Val Glu Asn Tyr Arg Arg His Ile 695 Val Cys Val Ala Ile Phe Ser Ala Ile Cys Val Gly Val Phe Ala Asp 710 715 Arg Ala Tyr Tyr Gly Phe Ala Leu Pro Pro Ser Asp Ile Ala Gln 725 730 Thr Thr Leu Val Gly Ile Ile Leu Ser Arg Gly Thr Ala Ala Ser Val Ser Phe Met Phe Ser Tyr Ile Leu Leu Thr Met Cys Arg Asn Leu Ile Thr Phe Leu Arg Glu Thr Phe Leu Asn Arg Tyr Val Pro Phe Asp Ala 770 Ala Val Asp Phe His Arg Trp Ile Ala Met Ala Ala Val Val Leu Ala 790 795 Ile Leu His Ser Ala Gly His Ala Val Asn Val Tyr Ile Phe Ser Val 805 815 Ser Pro Leu Ser Leu Leu Ala Cys Ile Phe Pro Asn Val Phe Val Asn 825 Asp Gly Ser Lys Leu Pro Gln Lys Phe Tyr Trp Trp Phe Phe Gln Thr 840 Val Pro Gly Met Thr Gly Val Leu Leu Leu Val Leu Ala Ile Met 850 855 Tyr Val Phe Ala Ser His His Phe Arg Arg Arg Ser Phe Arg Gly Phe 870 875 Trp Leu Thr His His Leu Tyr Ile Leu Leu Tyr Ala Leu Leu Ile Ile 885 His Gly Ser Tyr Ala Leu Ile Gln Leu Pro Thr Phe His Ile Tyr Phe Leu Val Pro Ala Ile Ile Tyr Gly Gly Asp Lys Leu Val Ser Leu Ser 920 Arg Lys Lys Val Glu Ile Ser Val Val Lys Ala Glu Leu Leu Pro Ser 930 Gly Val Thr Tyr Leu Gln Phe Gln Arg Pro Gln Gly Phe Glu Tyr Lys 945 955 950

199

Ser Gly Gln Trp Val Arg Ile Ala Cys Leu Ala Leu Gly Thr Thr Glu 965 970 975

Tyr His Pro Phe Thr Leu Thr Ser Ala Pro His Glu Asp Thr Leu Ser 980 985 990

Leu His Ile Arg Ala Val Gly Pro Trp Thr Thr Arg Leu Arg Glu Ile 995 1000 1005

Tyr Ser Ser Pro Lys Gly Asn Gly Cys Ala Gly Tyr Pro Lys Leu Tyr 1010 1015 1020

Leu Asp Gly Pro Phe Gly Glu Gly His Gln Glu Trp His Lys Phe Glu 1025 1030 1035 1040

Val Ser Val Leu Val Gly Gly Gly Ile Gly Val Thr Pro Phe Ala Ser 1045 1050 1055

Ile Leu Lys Asp Leu Val Phe Lys Ser Ser Leu Gly Ser Gln Met Leu 1060 1065 1070

Cys Lys Lys Ile Tyr Phe Ile Trp Val Thr Arg Thr Gln Arg Gln Phe 1075 1080 1085

Glu Trp Leu Ala Asp Ile Ile Gln Glu Val Glu Glu Asn Asp His Gln 1090 1095 1100

Asp Leu Val Ser Val His Ile Tyr Val Thr Gln Leu Ala Glu Lys Phe 1105 1110 1115 1120

Asp Leu Arg Thr Thr Met Leu Tyr Ile Cys Glu Arg His Phe Gln Lys 1125 1130 1135

Val Leu Asn Arg Ser Leu Phe Thr Gly Leu Arg Ser Ile Thr His Phe 1140 1145 1150

Gly Arg Pro Pro Phe Glu Pro Phe Phe Asn Ser Leu Gln Glu Val His 1155 1160 1165

Pro Gln Val Arg Lys Ile Gly Val Phe Ser Cys Gly Pro Pro Gly Met 1170 1175 1180

Thr Lys Asn Val Glu Lys Ala Cys Gln Leu Val Asn Arg Gln Asp Arg 1185 1190 1195 1200

Ala His Phe Met His His Tyr Glu Asn Phe 1205 1210

<210> 693

<211> 277

<212> PRT

<213> Homo sapiens

<400> 693

Met Ala Tyr Gln Asp Leu His Ser Glu Ile Thr Ser Leu Phe Lys Asp
5 10 15

200

Val Phe Gly Thr Ser Val Tyr Gly Gln Thr Val Ile Leu Thr Val Ser 20 25 30

Thr Ser Leu Ser Pro Arg Ser Glu Met Arg Ala Asp Asp Lys Phe Val 35 40 45

Asn Val Thr Ile Val Thr Ile Leu Ala Glu Thr Thr Ser Asp Asn Glu 50 55 60

Lys Thr Val Thr Glu Lys Ile Asn Lys Ala Ile Arg Ser Ser Ser 65 70 75 80

Asn Phe Leu Asn Tyr Asp Leu Thr Leu Arg Cys Asp Tyr Tyr Gly Cys
85 90 95

Asn Gln Thr Ala Asp Asp Cys Leu Asn Gly Leu Ala Cys Asp Cys Lys
100 105 110

Ser Asp Leu Gln Arg Pro Asn Pro Gln Ser Pro Phe Cys Val Ala Ser 115 120 125

Ser Leu Lys Cys Pro Asp Ala Cys Asn Ala Gln His Lys Gln Cys Leu 130 135 140

Ile Lys Lys Ser Gly Gly Ala Pro Glu Cys Ala Cys Val Pro Gly Tyr 145 150 155 160

Gln Glu Asp Ala Asn Gly Asn Cys Gln Lys Cys Ala Phe Gly Tyr Ser 165 170 175

Gly Leu Asp Cys Lys Asp Lys Phe Gln Leu Ile Leu Thr Ile Val Gly
180 185 190

Thr Ile Ala Gly Ile Val Ile Leu Ser Met Ile Ile Ala Leu Ile Val 195 200 205

Thr Ala Arg Ser Asn Asn Lys Thr Lys His Ile Glu Glu Asn Leu 210 215 220

Ile Asp Glu Asp Phe Gln Asn Leu Lys Leu Arg Ser Thr Gly Phe Thr 225 230 235 240

Asn Leu Gly Ala Glu Gly Ser Val Phe Pro Lys Val Arg Ile Thr Ala 245 250 255

Ser Arg Asp Ser Gln Met Gln Asn Pro Tyr Ser Arg His Ser Ser Met 260 265 270

Pro Arg Pro Asp Tyr 275

<210> 694

<211> 157

<212> DNA

<213> Homo sapien

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<400> 694
aaatataaat gatatgttga aaacttaagg aagcaaatgc tacatatatg caatataaaa
                                                                         60
tagtaatgtg atgctgatgc tgttaaccaa agggcagaat aaataagcaa aatgccaaaa
                                                                        120
ggggtcttaa ttgaaatgaa aatttaattt tgttttt
                                                                        157
<210> 695
<211> 241
<212> DNA
<213> Homo sapien
<400> 695
ctggcccgac ctctggcctc ctcttccctg gctgaatgta aatatttacc agcatttaga
                                                                         60
aaaaaggaga aaaaagacag aactaaaccc gtttaggaaa aagggaccga gggacagcag
                                                                        120
tggttaagta atccactgag gacctgaagg ggaaaatgga cttacctttc tcatatactt
                                                                        180
ggcctggcta ggacactggg tgccagacag ccttctgagg ggattttctt tctaaatgag
                                                                        240
                                                                        241
<210> 696
<211> 188
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(188)
<223> n = A, T, C or G
<400> 696
gcccatgatg ncagagctgg aagagagnn acgtcagcag aggggccacc tccatttgnt
                                                                         60
gnagacaagc atagatggga ttctggctga tgtgaagaac ttggagaaca ttagggacaa
                                                                        120
cctgccccca ggctgctaca atacccaggc tcttgagcaa cagtnaagct gccataaata
                                                                        180
tttctcaa
                                                                        188
<210> 697
<211> 289
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(289)
<223> n = A, T, C or G
<400> 697
ctgcttggac ttcaaagccc tccgcctagc catctcagcc aggctcaggn tccttctccc
                                                                         60
acceateagg ceaageagga cttgtnaaac atacacatte aagtteetag cacacagtag
                                                                        120
gtgctaagtg ggaattgatt ataaacttga attcttccat caacaaatat ctacctctcc
                                                                        180
tgtccagctt gcctcagatc ttcaggntct ctcttctctg aggcagctaa gcttctacat
                                                                        240
ccttcatgaa gtttccttta cttctcgaca gaagacagtt ccctttagg
                                                                        289
<210> 698
<211> 193
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(193)
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<223> n = A, T, C or G
<400> 698
                                                                         60
aaagtttgtg ctataaaatt gtgcaaatat gttaaggatt gagacccacc aatgcactac
tgtaatattt cgcttcctaa atttcttcca cctacagata atagacaaca agtctgagaa
                                                                        120
                                                                        180
actaaggcta accaaactta gatataaatc ctaccaataa aatttttcag ntttaagttt
tacagtttga ttt
                                                                        193
<210> 699
<211> 279
<212> DNA
<213>.Homo sapien
<220>
<221> misc_feature
<222> (1)...(279)
<223> n = A, T, C or G
<400> 699
ccttccccc ccttccttat gagttctaac ttagtaattt caaatgtgac cttttatatn
                                                                         60
taagaccagt atagtaaact tagcccacag tggcaaataa tgagtaatat tgtaatatgt
                                                                        120
tccagnggga taccctcctt gtcttgaatt ttggctttga cattctcaat ggtgtcactg
                                                                        180
                                                                        240
ggetegacet caagggtgat ggttttgeca gtgagggtet teacaaagat etgeatgttt
                                                                        279
gcgtccgcac gaccgccgcc accaaccagc tcggccgcc
<210> 700
<211> 340
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(340)
<223> n = A, T, C or G
<400> 700
ctgtccaatg acaacaggac cctcactcta ctcagtgtca caaggaatga tgtaggaccc
                                                                         60
                                                                        120
tatgagtgtg gaatccagaa caaattaagt gttgaccaca gcgacccagt catcctgaat
                                                                        180
gteetetatg geecagaega eeceaceatt teeceeteat acaeetatta eegneeaggg
                                                                        240
gtgaacctca gcctctcctg ccatgcagcc tctaacccac ctgcacagta ttcttggctg
                                                                        300
attgatggga acatccagca acacacaa gagctcttta tctccaacat cactgagaag
aacagcggac tctatacctg ccaggccaat aactcagcca
                                                                        340
<210> 701
<211> 277
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(277)
<223> n = A, T, C or G
<400> 701
ccactggctg agntattggc ctggcaggna tagagtccgc tgttcttctc agtgatgttg
                                                                         60
gagataaaga gctcttgtgt gtgttgctgg atgttcccat caatcagcna agaatantgt
                                                                        120
gcaggtgggt tagaggctgc atggcaggag aggctgaggt tcacccctgg acggtaatag
                                                                        180
gngtatgagg gggaaatggt ggggtegtet gggccataga ggacatteag gatgaetggg
                                                                        240
```

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tcgctgtggt caacacttaa tttgttctgg attccac
                                                                         277
 <210> 702
 <211> 255
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(255)
 <223> n = A, T, C or G
 <400> 702
 ctgcgcgtcg ccaaagtgac aggcggngcg gcctccaagc tntctaagat ccgagtcgtc
                                                                          60
 cggaaatcca ttgcccgtgt tctcanagtt attaaccaga ctcagaaaga aaacctcagg
                                                                         120
 aaattetaca agggcaagaa gtacaageee etggacetge ggeetaagaa gacaegtgee
                                                                         180
 atgcgccgcc ggctcaacaa gcacgaggag aacctgaaga ccaagaagca gcagcggaag
                                                                         240
 gagcggctgt acccg
                                                                         255
 <210> 703
 <211> 224
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc feature
 <222> (1)...(224)
<223> n = A, T, C or G
<400> 703
 cctgtttgga ggngctgctc gaaagggttt gccctgagac tnnaagaaga agctgcggga
                                                                          60
 aggacagcag gggncctggg gttttagcnt ctggcccagg agttatgtgt ccataaccaa
                                                                         120
agggagcaca gtctgcaccc agctctcatc ccatcggagc tqctqcqact cccqcaggnt
                                                                         180
 cttccggaac tggtttagct tgcccgcagn atcagnaaag tttg
                                                                         224
<210> 704
<211> 445
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(445)
<223> n = A, T, C or G
<400> 704
aggtaaaaag cagcctgggc aagagaagtg ggtgggttta ggagaatccc tttcgaaaaa
                                                                         60
ttcagagcat tattattaat ccttcttaaa ttaaatgcag ggccaagcat gctgcacgtg
                                                                         120
gaatctggac aattttttga taaactttaa ggctgctaaa taatttacag aaactgtgaa
                                                                         180
tgcattttca ttttacgagg caaaagagaa aatattcaag attgcatagc aattttattt
                                                                         240 -
tttgaaatgg ntatcctaaa gaatttcctt aaattcagat tttgcaaaat tcctactctc
                                                                         300
caagtcatca agngaacact aaaagcaact ttactcgtga atacagggga ctctttacga
                                                                         360
ggcatgcatt tttcataaat ctaggccaaa gngaactaat tgagatttaa ttctaaattc
                                                                         420
atcctgngat ttctgcatat aatat
                                                                         445
<210> 705
<211> 107
<212> DNA
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<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A, T, C or G
<400> 705
atcacccnat ttaattaaaa atccctggnc tnaggaccta cagcanngta ctgnagaact
                                                                          60
tnagaacctn aattagccat ttgccatctt nagagagtct tnnccat
                                                                         107
<210> 706
<211> 113
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1) ... (113)
<223> n = A, T, C or G
<400> 706
aaatagtttc taaaggcaag gncttgctat gttgcttagg ctggttttga aaagtccctt
                                                                         60
                                                                        113
ttggggggat gctttcactg cttcacttcc tttctatgac agctnaggga atc
<210> 707
<211> 283
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(283)
<223> n = A, T, C or G
<400> 707
ctgctccaag gccatcaaga tcttcatggg gaggacggag ctgaagntgg aagacaagca
                                                                         60
ccgtgtggtg atccagcgtg atgagggtca ccacgtggcc tacaccacgc gggaggtggg
                                                                        120
                                                                        180
ccagtanctg gnggnggagt ccagcacggg catcatcgnc atctgggaca agaggaccac
cgtgttcatc aagctggctc cctcctanaa gggcaccgtg ngnggcctgt gtgggnactt
                                                                        240
                                                                        283
tgaccaccgc tccaacaacg acttcaccac gcgggnccac atg
<210> 708
<211> 341
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(341)
<223> n = A, T, C or G
<400> 708
ctgtccaatg acaacaggac cctcactcta ctcagtgtca caaggaatga tgtaggaccc
                                                                         60
tatgagtgtg gaatccagaa caaattaagt gttgaccaca gcgacccagt catcctgaat
                                                                        120
gtcctctatg gcccagacga ccccaccatt tccccctcat acacctatta ccqtccaqqq
                                                                        180
gngaacetca gcctctcctg ccatgcagec tctaacccac ctgcacagta ttcttggctg
                                                                        240
                                                                        300
attgatggga acatccagca acacacacaa gagctcttta tctccaacat cactgagaag
```

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aacagcggac tctatacctg ccaggccaat aactcagcca g
                                                                        341
<210> 709
<211> 376
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(376)
<223> n = A, T, C or G
<400> 709
ccaagtccag gggcgtggag gccgcccggg agcggatgtt caatggtgag aagatcaact
                                                                         60
anaccgaggg tcgagccgtg ctgcacgtgg ctctgcggaa ccggtcaaan acacnnatcc
                                                                        120
tggtagacgg caaggatgtg atgccagagg tcaanaaggt tctgganaag atgaagtctt.
                                                                        180
tetgecageg tgteeggage ggngaetgga aggggtanae aggeaagaee ateaeggaeg
                                                                        240
tcatcaacat tggcattggc ggctccgacc tgggacccct catggngact gaagccctta
                                                                        300
agtcatactc ttcaggaggn ccccgcgnct gggatgnctc caacattgat ggaactcaca
                                                                        360
ttgccaaaac cctggc
                                                                        376
<210> 710
<211> 232
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(232)
<223> n = A, T, C or G
<400> 710
ctgctgtata ttcagcattg tgggaggagc tgtgaaagac anagaacagt anagggtgtg
                                                                         60
gnccctgccc tcgagaggnt tanagtctag gtggagaaac gggaancagg acacatgggg
                                                                        120
agccgagaga aaanagtcca ggccagtatg ttacaggagc tggaaggtgt ttggggtcag
                                                                        180
accccaatac tccaagtaca ctaagcactt cagtgcctcc aggggctcaa cg
                                                                        232
<210> 711
<211> 317
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(317)
<223> n = A, T, C or G
<400> 711
caggtaaaat agatttaatt taggaaagct cattttatat gagtttccaa ctaattatta
                                                                         60
gagtcagaaa caaagaaaat aaaatcagag aaaatcctct gtagaaaaaa tacacaaaga
                                                                        120
acatttctac atgtgaaaaa acagtaaaca gtgttaacat ccaagttatt agtctcaatt
                                                                        180
ccacgtetec tagtgaacac cactateaac ettgagatet gatttgntet tgteattett
                                                                        240
cactgagtag atgaaatatg ttaaggtgtc tttttcattc actggaatag acctaaagtg
                                                                        300
gcaaccaact atctcaa
                                                                        317
<210> 712
<211> 154
<212> DNA
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<213> Homo sapien
<220>
<221> misc feature
<222> (1) ... (154)
<223> n = A, T, C. or G
<400> 712
tntgtagaaa aaatanacaa agaacatttn tanatgtgaa aaaacagtaa acagngttaa
                                                                          60
catecaagtt attagtetea attecaegte teetagtgaa caccaetnte aacettgaga
                                                                         120
tctgatttgn tcttgtcatt cttcactgag taga
                                                                         154
<210> 713
<211> 177
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(177)
<223> n = A, T, C or G
<400> 713
                                                                          60
ccattcagag gtagaagatg gaggggcggc agattctggc agggcagcag agggctctat
                                                                         120
gcacgggttt caaacctgtt ttccacactc tgtctttgca gntttggtaa ttctgtggtc
tatttatana gatattaaaa tottgtttat aaaaaaaaa aaaaaaaaa aaaaaaa
                                                                         177
<210> 714
<211> 216
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G
<400> 714
                                                                          60
ctgtgtttcg gctataaaaa ggcggctgaa agaaggggaa aattanttta gacttaattg
                                                                         120
gaagtttcat atggcacaca ttaccagnag agaaaaaagat ataaacggca ataaatatta
ggctcgattt gagaaactct ccccacctca atgctttctt ttcccttgct atttaagggt
                                                                         180
                                                                         216
ctactttgca acccgtgtgn gtgtttgtgt gtgtgt
<210> 715
<211> 376
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(376)
<223> n = A, T, C or G
<400> 715
ctgtgcgagt gtaccggatg cttccacctc tcaccaagaa ccagagaaaa gaaagaaagt
                                                                         60
cgaagtccag ccgagatgct aagagcaagg ccaagaggaa gtcatgtggg gattccagcc
                                                                         120
ctgatacett ctctgatgga ctcagcaget ccactctgcc tgatgaccae agcagetaca
                                                                        180
                                                                        240
cagttccagg ctacatgcag gacttggagg nggagcaggc cctgactcca gctacaacag
```

atgaggatga ggaagggaaa ggcagccaac aagcgtggat cctctgtcta tggaga	ttacctgagg gggaaggggt	acatcatgaa acntactcaa	gctcttggag tgaacctgga	cagncggagt gnccagccca	300 360 376
<210> 716 <211> 96 <212> DNA <213> Homo sapien					
<220> <221> misc_feature <222> (1)(96) <223> n = A,T,C or G					
<400> 716 aaacttttta tttgcatatt aaaaaaaaat ggcnctntga			taattaaaat	catttgaana	60 96
<210> 717 <211> 366 <212> DNA <213> Homo sapien					
<220> <221> misc_feature <222> (1)(366) <223> n = A,T,C or G					
<400> 717 gatggaaagg atacagatga agtatcatac tggatgccat gcaaaagatc gagatcctga cagaatcaga gtggtgaaca gagtcttctg aggaaaattc gacaatgctg caagcatttc actaca	ccgggaatat aatggaaaat gatttcatca tctaaattct	gaggaggtag gaagaacaac agttctcagg cacccagaat	aagngctcct catcctctga aggntgattt cattatctct	ctctgataaa aaatgattct ggntgatcaa agcagatatg	60 120 180 240 300 360 366
<210> 718 <211> 200 <212> DNA <213> Homo sapien					
<220> <221> misc_feature <222> (1)(200) <223> n = A,T,C or G					
<400> 718 aaacatctca catatanaaa gcttctgtgg aaccatggaa tgaagaagat ttgggcaaat aatgctaaat caaattttt	gaagatgaaa	atgagactgg	caaagaacaa	atgctgaatc	60 120 180 200
<210> 719 <211> 336 <212> DNA <213> Homo sapien					

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·<220>
<221> misc feature
<222> (1)...(336)
<223> n = A, T, C or G
<400>. 719
                                                                          60
ctgtctcaca ctttgcaagc tgtgagagac acatcagagc cctgggcact gtcactgctt
                                                                         120
gcagcetgag ngtaactece teetttteta tetgagetet teeteeteea cateaeggea
gcgaccacag ctccagtgat cacagctcca aggagaacca ggccagcaat gatgcccacg
                                                                         180
                                                                         240
atggggatgg tgggctggga agacagctcc catctcaggg tgaggggctt gggcagaccc
                                                                         300
teatgetgea catggeaggn gtatetetge teeteteeag aaggeaceae cacageegee
                                                                         336
cacttctgga aggntccatc cccttgcagg ccttgg
<210> 720
<211> 167
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(167)
<223> n = A, T, C or G
<400> 720
ggagagtgct agtgaggcgg ccaagaagta natggaggag aatgannagc tcaagaaggg
                                                                         60
agctgctgtt gacggaggca agttggatgt cgggaatgct gaggtgaagt tggaggaaga
                                                                         120
gaacaggagc ctgaaggctg acctgcagaa gctaaaggac gagctgg
                                                                         167
<210> 721
<211> 134
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(134)
<223> n = A, T, C or G
<400> 721
cctagtatga ggagcgttat ggagtggaag tgaaatcana tggctaggcc ggaggncatt
                                                                         60
                                                                         120
aggagggctg agagggcccc tgttaggggt catgggctgg gntttacgtg cgtgaggagg
                                                                         134
ggcggagctt gcag
<210> 722
<211> 353
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(353)
<223> n = A, T, C or G
<400> 722
aaaaatatat acaactatga tgttcaaata tgtattctga gccattatgt tcaaacataa
                                                                         60
atatctggga aattcaaact gctgcaacaa gttaggaaag gattaaggaa aaatgatgag
                                                                         120
ctacaaatta tgtagttgga ggaagaaaaa aatgttactt agcatttatg tctggatagg
                                                                         180
tatgtatttt ctaatttaca tacacatatc cagntgagta tagacaacca tcaaaatgta
                                                                         240
```

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accagttaca cagagactag actaagccaa cactattttc tataacaggn aacagtagng
                                                                        300
atttcaaaaa ttttaatatc tcaatagttt caccaaaaat tatttatggg aat
                                                                        353
<210> 723
<211> 268
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(268)
<223> n = A,T,C or G
<400> 723
ctgagaagag cgccaggaag ccctgggtgc gagagttgat gacgtcgatc tcgtgcaggg
                                                                         60
acacggngtg caccacctcc ttgcgtttct ggagctcccc atctgggcac tgcacgaact
                                                                        120
tggnctggga gcccatagcg tcgtagtcgc gggcgngtgt gaaggagcgg cccaacttgg
                                                                        180
agatettgcc cgtcgccttg tcgatggnga tcacgtcccc ggcctggacc ttgtccttgg
                                                                       240
neagggacte aatcatettg ntgcccag
                                                                       268
<210> 724
<211> 344
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(344)
<223> n = A, T, C or G
<400> 724
aaagaatcag caaaatttca aataaaaaat tatqaaaata ttatcctcat taqttcattt
                                                                        60
agnoccatga aattaattat tttototgot ogatottggt ggacagttto atgaagotgt
                                                                       120
cagttagttc attaaagttt tggaaattct cagacagtgc agtggtatca gaaacttgta
                                                                       180
ttcaagagta naggtcagag ncttcttttc ttttcttttt gagatggagt cttgctctgt
                                                                       240
tgccagactg gagtgcagtg gtgcgatctg ggctcactgc aatctccacc tcccgggttc
                                                                       300
aagcgattet cetgeeteag cetecegagt aactgggaet acag
                                                                       344
<210> 725
<211> 345
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(345)
<223> n = A, T, C or G
<400> 725
aaacaagaga aagtagacag atacatgttg gnaaatgcta actgtccata ttcacataga
                                                                        60
gacacagtgt actctctgag cccaatatan agagaaagga ggaaaaaagc tagaattcta
                                                                       120
tgcactacta cacaggggcc tagcaccctc cagcttccag cagagcgaag ggagcaggnt
                                                                       180
tttctttttt cccacagagc tcggggggtt gattccatac agnttttgtt cagacaggaa
                                                                       240
gggataaaaa tgaacttcga acagaaaggg gtagagactc ttttcccatt gtattctgct
                                                                       300
caaggnattt cccccaaat aaattgagaa ccatggagnn gagaa
                                                                       345
<210> 726
<211> 305
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<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(305)
<223> n = A, T, C or G
<400> 726
                                                                         60
ttgcctgatg tcagagcccc tccacacatg agcctgctcc ctactgccaa caccgtggcc
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cagacagaga cgctttccga ggaagaggtg aagctcctgc agtcgctgaa gnaagganag
                                                                        180
cagateqtga ggaaaaaggg egeegaggtt gggggcatgt etetettett accaagetag
                                                                        240
actgggntgc cttttctaac tattccagcc ctacagggcg aggggccata atggagtatc
ccgccccttt agaccccagg cgctcaccgg cagggcaaga aggngaaatc cagcagccgc
                                                                        300
                                                                        305
gccag
<210> 727
<211> 387
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(387)
<223> n = A, T, C or G
<400> 727
ccaacgaggc atcacctctg acggtgtcag tcatcgatga ccggctcaag gagaagatgg
                                                                         60
tggtggagtt ccqccacatg aggaaccatg cctatgagcc actcgccagc ttcctagact
                                                                        120
tcattactta nagttacatg atcgacaacg ngatcctgct catcacaggc acgctgcacc
                                                                        180
agggetecat egetgagete gtgeecaagt gecacceact aggeagette gageagatgg
                                                                        240
aggeogtgaa cattgeteag acacetgetg agetetacaa tgecattetg gtggacaege
                                                                        300
                                                                        360
ctcttgcggc ttttttccag gactgcattt cagagcagga ccttaacgag atgaacatcg
                                                                        387
agatcatccg caacaccctc tacaagg
<210> 728
<211> 109
<212> DNA
<213> Homo sapien
<400> 728
ctgactgaca gccagattgc agatgtggct cgcttttgta accgctaccc taatatcgaa
                                                                         60
ctatcttatg aggtggtaga taaggacagc atccgcagtg gcgggccag
                                                                        109
<210> 729
<211> 32.9
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(329)
<223> n = A, T, C or G
<400> 729
aaagcatagg actatagtca gcatgctaga ctgagaggta aacactgatg caattagaac
                                                                         60
                                                                        120
aggtactgat gctgtcagtg tttaacacta tgtttagctg tgtttatgct ataaaagtgc
                                                                        180
aatattagac actagctagt actgctgcct catgtaactc caaagaaaac aggatttcat
```

211

taagtgcatt gaatgtggct atttctctaa gttactcata ttgtcctttg cttgaatgca 240 atgccgngca gatttatgtg gctgctattt ttattttctg ngcattactt taacacctta 300 aagngagaag caaacatttc cttcttcag 329 <210> 730 <211> 238 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(238) <223> n = A,T,C or G<400> 730 aaaaagtggc agagtgactt aactgatcat gcatgatccc tcatccctga aattgagttt 60 atgtagncat tttacttatt ttattcatta gctaactttg tctatgtata tttctagata 120 ttgattagtg taatcgatta taaaggatat ttatcaaatc cagggattgc attttgaaat 180 tataattatt ttctttgctg aagnattcat tgtaaaacat acaaaataaa catatttt 238 <210> 731 <211> 297 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(297) $\langle 223 \rangle$ n = A, T, C or G <400> 731 aaactgaatt ttttgacctt ggaaaatatt tttcttactt taccaaggtg aagtttcctt 60 aattagacta attattttat ccccatccca gggtataaac aggaattgtt ttgatagtgg 120 tggagttatt cactgcaaca aagcaacaat gttgtccatg attcaaaatc taagcagttt 180 cgattttgcc tgtgaatatg gngtctgtca ttcagggcat agctcactgt aggctagcct 240 ctgcttactt aagnetette tetgacatae teaatggaag aatatttaga tttattt 297 <210> 732 <211> 370 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(370) <223> n = A, T, C or G<400> 732 ctgtcagtct tcctgaaatg aagaaactac accagggctg ctatatcaga gcaaccccaa 60 ccagcactcc aatcatgatg ccgacagngg ccccaattag aagntcaaaa acaaaaatta 120 agttaggtag ncagacatct ataaatacta qtatccgcat qaatqaaaac accctggctt 180 tggnatggct acagaaatcc atctggaaat tattcaaaag gacgtggttc agggaaaagg 240 gggtaggcag ggcatggggg gaggggaaca cacaaaaccc ccaagcagag gtaaaatgaa 300 tattggaaca cacccgcagc aaacactgta catagacttg aggcagatgc ctctaacaca 360 acacatatac 370 <210> 733

<211> 733 <211> 242

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<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(242)
<223> n = A, T, C or G
<400> 733
cctcctattt attctagcca cctctagcct agccgtttac tcaatcctct gatcagggtg
                                                                          60
agcatcaaac tcaaactacg ccctgatcgg cgcactgcga gcagtagccc aagcaatctc
                                                                         120
atatgaagnc accctagcca tcattctact atcaacatta ctaataagtg gctcctttaa
                                                                         180
cctctccacc cttatcacaa cacaagaaca cctctgatta ctcctgccat catgaccctt
                                                                         240
                                                                         242
gg
<210> 734
<211> 368
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(368)
<223> n = A, T, C \text{ or } G
<400> 734
cctttcttgt aagtgaagaa aaaggaatgc agcaaagaag agttcgacat tggagtcctt
                                                                          60
agttccatca ggatcccatt cgcagccttt agcatcatgt agaagcaaac tgcacctatg
                                                                         120
gctgagatag gtgcaatgac ctacaagatt ttgngttttc tagctgtcca ggaaaagcca
                                                                         180
tcttcagnct tgctgacagt caaagagcaa gtgaaaccat ttccagccta aactacataa
                                                                         240
aagcagccga accaatgatt aaagacctct aaggctccat aatcatcatt aaatatgccc
                                                                         300
aaactcattg ngacttttta ttttatatac aggattaaaa tcaacattaa atcatcttat
                                                                         360
                                                                         368
ttacatgg
<210> 735
<211> 308
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(308)
<223> n = A, T, C or G
<400> 735
ctgtccaata ggcgtagcta tccggacaga gcacgtttgc agaaggggga ctcttcttcc
                                                                          60
aggtagetga aaggggaaga cetgaegtae tntggttagg ntaggaettg ceetegtggn
                                                                         120
ggaaactttt cttaaaaagt tataaccaac ttttctatta aaagtgggaa ttaggagaga
                                                                         180
aggtaggggt tgggaatcag agagaatggc tttggnctct tgcttgtggg actagcctgg
                                                                         240
cttgggacta aatgccctgc tctgaacacg aagcttagna taaactgatg gatatcccta
                                                                         300
ccttgaaa
                                                                         308
<210> 736
<211> 354
<212> DNA
<213> Homo sapien
<220>
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<221> misc_feature
<222> (1)...(354)
<223> n = A,T,C or G
<400> 736
cettetgeta egtagtetae aacagaagga tteaggeaat tacetetgee atgeggngga
                                                                         60
acatgggttc atacaaactc ttcttaaggt aaccctggaa gtcattgaca cagagcattt
                                                                        120
ggaagaactt cttcataaag atgatgatgg agatggctct aagaccaaag aaatgtccaa
                                                                        180
tagcatgaca cctagccaga aggtctggta caqaqacttc atgcaqctca tcaaccaccc
                                                                        240
caatctcaac acgatggatg agttctgtga acaagtttgg aaaagggacc gaaaacaacg
                                                                        300
teggeaaagg ceaggacata eeceagggaa cagtaacaaa tggaagcact taca
                                                                        354
<210> 737
<211> 198
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(198)
<223> n = A, T, C or G
<400> 737
ctgecgetge acacgetegt tettetetge etcagtgatg egetteteet cattgeggne
                                                                         60
atcccggatg ccctcactag acagetecge getgtagece gtgggetetg egeceteate
                                                                        120
ctgcaagctc tcctggacat ggtagctcac cggctcgtac acggggggtg gtggggcgg
                                                                        180
gggngctgtc atcaccag
                                                                        198
<210> 738
<211> 228
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(228)
<223> n = A, T, C or G
<400> 738
gtgccatggc acacagcctg ggtgcacacc cagcgncctc tcttgcaggt gcaggtattg
                                                                         60
cagtccacct tgatcttggc gccggaagaa tanaggtcgt tgttatggac gcaagggcat
                                                                        120
tectteteca ecaegeagee acceeggeeg teatecatea geeegteggg geacaeaaag
                                                                        180
ccactgacac actctgtgtg gnaatagccg gcggccagcg nctggcag
                                                                        228
<210> 739
<211> 378
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(378)
<223> n = A, T, C or G
<400> 739
aaaaaataca ggagtcgata gcagcagttg gtgacgagat ggcactcaga aacggcgttg
                                                                         60
acgtaattta ggacgtggaa tcataagcga aacagcacac tgtttgaata aagagcgagt
                                                                        120
cggnatttat atttgntttt cttttgtcat gattatttga tttttaagnt gctccagcta
                                                                        180
```

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aggcattttt ttgtattagn atttctatta qqqaaccttt cttattagqn qqnttqtatt
                                                                        240
                                                                        300 .
gtctggnttc taacatgcag gtagctgttt ggcagttaaa cacgtttaga gtaatttgag
ttacaacgtg tgaaactgag caaaaaagca gngataagnt tgggttacca taccaaatat
                                                                        360
ttgttttccc actggaaa
                                                                        378
<210> 740
<211> 200
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(200)
<223> n = A, T, C or G
<400> 740
ccacttgagt ggntcctggc tgcttctgtg attgttaggt cttgagagat tatggacccg
                                                                         60
aggeattetg ggtaceceat caattggetg atggnettet atttgggetg egettettet
                                                                        120
aaaaagggga gctcaaaggt cttttttcc cccactgcag agctaaaaaa gtccctgtac
                                                                        180
gccatcttct cccagtttgg
                                                                        200
<210> 741
<211> 273
<212> DNA
<213> Homo sapien
<400> 741
ctgcttggca tcgtaatggg ccggtggcat catgagcccc agaatcagcc ttgccaggtc
                                                                         60
tccagagatc tcagacttca ggtcagtcat taagtcccgg ccaaagtgag acttgaaggt
                                                                        120
ctgccggatc tgctgccgct ggacattgct gcggtgcgtg atgatatcga tgattgtgtc
                                                                        180
ttcgtcagtc ccgagtccct tcatggcttt ccgcagcgct ttggcatctg cgtcagggtt
                                                                        240
gaagtcattg gctgggcgca caggtccctt cag
                                                                        273
<210> 742
<211> 297
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(297)
<223> n = A, T, C or G
<400> 742
ctgcagttgc tccctttagg gttataaaat aatgacccaa atgttacatg tgttgatatt
                                                                         60
ataacttgtc agttactgat gtctgtggna tcctaccctc atctctgaaa gggataatac
                                                                        120
tgaataatta ttagaaaact ataaaacttc acactttgta ccattaaaac ctaaaatttt
                                                                        180
aatéttgnee ttttttaeta tggateagte ggeaeteggg aacageagea aggaaaagag
                                                                        240
gcaaatttca ttcacatgtt ctgngntcat acctcttctc tacctaattg ttcattt
                                                                        297
<210> 743
<211> 381
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(381)
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<223> n = A, T, C or G
<400> 743
ctgcacctcc acctccttga agttgaagat actattgcca tcaaagccag cagccagctc
                                                                         60
tggacagtat gcctgcaggg aacctccatg ccggctcagt gacacactct ctgcagccag
                                                                        120
ggtaatgaac ttgtcctcag ctacaaaagc tgtgagcttg gctgtgctca cctccagggt
                                                                        180
                                                                        240
taggtttagc agccgctttg ggggtaatgg ctcaggggca cggccttcta gctcagaagn
                                                                        300
agntectgaa gnetetagtg caagggatgg tacagtetca ggaaacacag nggetettag
                                                                        360
taggnetegg cactgtagag nggnggnate cecagagetg gngatgattt ggttgteate
                                                                        381
caggaagcgg caacacgaca g
<210> 744
<211> 167
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(167)
<223> n = A, T, C \text{ or } G
<400> 744
cagegngggg ctcggagagg tgctcggatt ctcgtagctg tgccgggact taaccaccac
                                                                         60
catgtcgagc aaaagaanaa agaccaagac caagaagcgc cctcagcgtg caacatccaa
                                                                        120
tgtgtttgct atgtttgacc agtcacagat tcaggagttc aaagagg
                                                                        167
<210> 745
<211> 96
<212> DNA
<213> Homo sapien
<400> 745
ccacaaactc ctctggctgt actccctcct gcaggagacc ggcctcactg cactcagcag
                                                                         60
                                                                         96
gctcttctcc ctgcgattca cttctgggac agtcac
<210> 746
<211> 391
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(391)
<223> n = A, T, C or G
<400> 746
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                                                                         60
gccgtcagca ggctgagatc cgtctctgag atgttgatgg ggatgtcggc agcagagccg
                                                                        120
acctttaggt gggacatacg catggagtcg tcacctgtga cccgggcagt gaaggggctg
                                                                        180
cctgggacgt gctgttcatt gtacttgact agaatgctgt agtcccccgg cagcacaggc
                                                                        240
aagtaggaca cgctgcnatg tcccatcctg gttgtcagtg cagtgttgct tgttcagtat
                                                                        300
ctcaagccca gaaagatgaa ttaatccttg aaggaaatga cattgagctt gtttcaaatt
                                                                        360
cagoggottt gattcagcaa gccacaacag t
                                                                        391
<210> 747
<211> 408
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(408)
<223> n = A, T, C or G
<400> 747
aaagttgttt gtgccttttt atttttgttt ttaatgcttt gatatttcaa tgttagcctc
                                                                          60
aatttctgaa naccataggt agaatgtaaa gcttgtctga tcgttcaaag catgaaatgg
                                                                        120
atacttatat ggaaattctg ctcagataga atgacagtcc gtcaaaacag attgcttgca
                                                                        180
aaggggaggc atcagtgtcc ttggcaggct gatttctagg taggaaatgt ggnagcctca
                                                                        240
cttttaatga acaaatggcc tttattaaaa actgagtgac tctatatagc tgatcagttt
                                                                        300
tttcacctgg aagcatttgt ttctactttg atatgactgt ttttcggaca gtttatttgt
                                                                        360
tgagagngtg accaaaagtt acatgtttgc acctttctag gtgaaaat
                                                                        408
<210> 748
<211> 337
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(337)
<223> n = A, T, C or G
<400> 748
ggcggagaga ggcgagcacc gggaagggga gcgnggggcc gctggaatgg gtgaatttaa
                                                                         60
ggnccatcga gtacgtttct ttaattatgt tccatcagga atccgctgtg tggcttacaa
                                                                        120
taaccagtca aacagattgg ctgtttcacg aacagatggc actgtggaaa tttataactt
                                                                        180
gtcagcaaac tactttcagg agaaattttt cccaggtcat gagnctcggg ctacagaagc
                                                                        240
tttgtgctgg gcagaaggac agcgactctt tagtgctggg ctcaatggcg agattatgga
                                                                        300
gnatgattta caggcgttaa acatcaagta tgctatg
                                                                        337
<210> 749
<211> 261
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(261)
<223> n = A, T, C or G
<400> 749
ccgggagget ctgattattt acccaccaca ggtaggttgt gttctgaatc tcaggttcac
                                                                         60
aggttaaggc tacagcatcc tcatcctcca cggggttgga gttgttgctg gngatgaagg
                                                                        120
gtttgggtgg ctctgcatag actgtgatcg ncgtgactgt ggncctattg aggccagtgt
                                                                        180
ctgagttatg ggcttggcac gtataggatc cactattatt cacagngatg ttggggataa
                                                                        240
agagetettg ggnggattge t
                                                                        261
<210> 750
<211> 150
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(150)
```

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<223> n = A, T, C or G
<400> 750
aacgetgang acatgacate caaagattae taetttgaet eetaegeaca etttgnnate
                                                                         60
cacgaggaga tgctgaagga cgaggtgcgc accctcactt accgcaactc catgtttcat
                                                                        120
aaccggcacc tcttcaagga caaggngnng
                                                                        150
<210> 751
<211> 288
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(288)
<223> n = A, T, C or G
<400> 751
aaaacttttg ttaagaaaaa ctgccagttt gtgcttttga aatgtctgtt ttgacatcat
                                                                         60
agtetagtaa aattttgaca gtgcatatgt actgttacta aaagetttat atgaaattat
                                                                        120
taatgtgaag nttttcattt ataattcaag gaaggatttc ctgaaaacat ttcaagggat
                                                                        180
ttatgtctac atatttgtgt gtgtgtgtgt gtatatatat gtaatatgca tacacagatg
                                                                        240
catatgtgta tatataatga aatttatgtt gctggnattt tgcatttt
                                                                        288
<210> 752
<211> 248
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(248)
<223> n = A,T,C or G
<400> 752
ctggcactga ggattatatc catataagaa ttcaacagag aaacggcagg aagaccctta
                                                                         60
ctactgtcca agggatcgct gatgattacg ataaaaagaa actagtgaag gcgtttaaga
                                                                        120
aaaagtttgc ctgcaatggt actgtaattg agcatccgga atatggagaa gtaattcagc
                                                                        180
tacagggnga ccaacgcaag aacatatgcc agttcctcgt agagattgga ctggctaagg
                                                                        240
acgatcag
                                                                        248
<210> 753
<211> 346
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(346)
<223> n = A, T, C or G
<400> 753
ctgctagaaa acagggaaga tattagccaa tatggaattg ccaggttctt cactgaatat
                                                                         60
tttaacagtg tatgccaggg aacacacatt ctctttcgag aattcagctt cgtccaagcc
                                                                        120
acccccaca atagggnatc atttttacgg gccttctgga gatgcttccg aactgtgggc
                                                                        180
aaaaatggcg atttgctgac catgaaagaa tatcactgtt tgctgcaatt actgtgtcct
                                                                        240
gatttcccgc tggagctcac tcagaaagca gccaggattg tgctcatgga cgatgccatg
                                                                        300
gactgcttga tgnctttttc agatttcctc tttgccttcc agatcc
                                                                        346
```

```
<210> 754
<211> 100
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1) ... (100)
\langle 223 \rangle n = A,T,C or G
<400> 754
gtgccacagg cagccctggg anataggaag ctgggagcaa ggaaagggtc ttagtcactg
                                                                          60
cctcccgaag ntgcttgaaa gcactcggag aattgtgcag
                                                                         100
<210> 755
<211> 405
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(405)
<223> n = A, T, C or G
<400> 755
tgtgggccca cttcccaaat ctctggagga tctgcagctt actcataaca agatcacaaa
                                                                          60
gctgggctct tttgaaggat tggtaaacct gaccttcatc catctccagc acaatcggct
                                                                         120
gaaagaggat gctgtttcag ctgcttttaa aggtcttaaa tcactcgaat accttgactt
                                                                         180
gagetteaat cagatageea gaetgeette tggneteeet gtetetette taacteteta
                                                                         240
                                                                         300
cttagacaac aataagatca gcaacatccc tgatgagtat ttcaagcgtt ttaatgcatt
gcagnatctg cgtttatctc acaacgaact ggctgatagt ggaatacctg gaaattcttt
                                                                         360
caatgngnca teeetggntg agetggatet gteetataac aaget
                                                                         405
<210> 756
<211> 306
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A, T, C or G
<400> 756
ccttgggaaa ttacctggaa atgcgactga aatcttcctt cctgaggggt ctgggctctt
                                                                          60
ggaaatcaaa ccctctcagg ttgggtggct ggacgattct cctcacactt anaatgggac
                                                                         120
aaggggaacc aggaggcccc caaggggatc cctgggntcc acacgaactc ctcctaccct
                                                                         180
cattgngtga cagcagccat gcctcctcct ggggatcagg atctattacc tgtgcctgga
                                                                         240
gaggagggga ctcctcttct cacccgctgg nctctggaca catactgtcc aattcccctg
                                                                         300
tggcag
                                                                         306
<210> 757
<211> 321
<212> DNA
<213> Homo sapien
<220>
```

```
<221> misc feature
 <222> (1)...(321)
 <223> n = A, T, C or G
 <400> 757
 ctggagggag gntccctggg aggtttttgt ggattccttc tgcagngact cccctggttt
                                                                          60
 ctggntctgg ggacccagng tccaggcgca gncttttagc acttctcagt gtagacgttg
                                                                         120
 acagggntet tttecegett gaateetget gagteeceaa atetettgae ttgtettggn
                                                                         180
 tacagncacc accagagetg etencagntt tgacaaaage agttgetget gaagngateg
                                                                         240
 ttttgaatcc tatcatagca ctggcaggtc ccggnaaatt cttacagtca gcaggcggac
                                                                         300
 ctcgtgtgag ttgaatattc c
                                                                         321
 <210> 758
 <211> 278
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc feature
 <222> (1)...(278)
<223> n = A, T, C or G
<400> 758
cgctcggcaa gntctcccag gagaaagcca tgttcagttc gagcgccaag atcntgaagc
                                                                         60
ccaatggcga gaagccggac gagttcgagt ccggcatctc ccaggctctt ntggagctgg
                                                                        120
agatgaactc ggacctcaag gctcagctna gggagctgaa tattacggca gctaaggaaa
                                                                        180
ttgaagttgg tggtggtcgg aaagctatca taatctttgn tcccgntcct caaacctgcc
                                                                        240
cgggcggccg cttcgagccc tatagtgagg cgnattag
                                                                        278
<210> 759
<211> 401
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(401)
<223> n = A, T, C or G
<400> 759
gcaaactgca aaccatggtg agaaattgac gacttcacac tatggacagc ttttcccaag
                                                                         60
atgtcaaaac aagactcctc atcatgataa ggctcttacc cccttttaat ttgtccttgc
                                                                        120
ttatgcctgc ctctttcgct tggcaggatg atgctgtcat tagtatttca caagaagtag
                                                                        180
cttcagaggg taacttaaca gagtatcaga tctatcttgt caatcccaac gttttacata
                                                                        240
aaataagaga teetttagtg cacceagnga etgacattag cagcatettt aacacageeg
                                                                        300
ngtgttcaaa tgtacagngg nccttttcag agntggactt ctagactcac ctgttctcac
                                                                        360
tccctgnttt aattcaaccc agccatgcaa tgccaaataa t
                                                                        401
<210> 760
<211> 346
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(346)
<223> n = A, T, C or G
```

```
<400> 760
ccgaggtttg gatcatggga gaacagcaga aaggggttat tgagggaacc tacactgttc
                                                                         60
tagctgcacc ccatgccctt ctcagaggaa agcctggcat tgattagata ctgggccaga
                                                                        120
ctaatactgg cagcagagcc agtgatagta acctgcctac cagaggagcc ttccactggg
                                                                        180
                                                                        240
ttggcaattt tgatctgggc cccggacatc tggcggatct cattaatgtt ggcgccttgg
cgcccgatta tgcagccaat taagttattt ggaatggnga gttcatgggt ggtttgagta
                                                                        300
gatgcatcca aacttgccca atagcctttc acctntggag agacct
                                                                        346
<210> 761
<211> 256
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(256)
<223> n = A, T, C or G
<400> 761
gagacagact gggtgatgac gctgaatctg cagaggtgct ggtgaccaat tcccctaaag
                                                                         60
catctacttg tctcctcaaa ctgtgtaaag tgccctctgt ctgccgcttt cctttaatta
                                                                        120
atacttctgc ttgcttggac atacagtgtc ggagttggnc ctgaaaagtg tgataagact
                                                                        180
                                                                        240
taggntttta cacagnaaga aatgtaccag aactgctgct cagcttcctc acatacattt
gataggcaaa tctagc
                                                                        256
<210> 762
<211> 321
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(321)
<223> n = A, T, C or G
<400> 762
tggactctgg antgatgctg gaagtagata cgaaaatgng aagaacaatg gaacagcaca
                                                                         60
ctttctggag catatggctt tcaagggcac caagaagaga tcccagttag atctggaact
                                                                        120
tgagattgaa aatatgggtg ctcatctcaa tgcctatacc tncagagagc agactgtata
                                                                        180
ctatgccaaa gcattctcta aagacttgcc aagagctgta gaaattcttg ctgatataat
                                                                        240
acaaaacagc acattgggag aagcagagat tgaacgtgag cgtggagtaa tccttagaga
                                                                        300
                                                                        321
gatgcaggaa gttgaaacca a
<210> 763
<211> 348
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(348)
<223> n = A, T, C or G
<400> 763
tgagaaaaca taaagtaacc agcagatttc aatattaaaa agaagtggtt cntcctaaaa
                                                                         60
aaggtnttag atcatagagt tgggattagg gtaggggata cctattaatc tggnctggaa
                                                                        120
aaaaagngtg tggagaaggg gagntgtatt gntttctcac aagaggcaaa cttcagncaa
                                                                        180
acaatgaaga gatagtaggn agggagatgt gtgntagacc aaagactttc tgattqctga
                                                                        240
```

```
taataacaaa tttagcagct ntctacaagt caattaaaat accattctct gagacatttt
                                                                        300
cagagaggag ctaactaaca cccacccagg nggaaaaatc attctaca
                                                                        348
<210> 764
<211> 374
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(374)
<223> n = A,T,C or G
<400> 764
agenaagaag gaageteetg eeecteetaa agetgaagee aaagegaagg etttaaagne
                                                                         60
caagaaggca gcgttgaaag gtgtccacag ccacaaaaag aagaagatcc ncacgtcacc
                                                                        120
cacctteeng engecgaaga cactgegaet eeggagaeag eecaaatate eteggaagag
                                                                        180
cgctcccagg agaaacangc ttgnccacta tgctatcatc aagtttccgc tgaccactga
                                                                        240
gnetgeeatg aagaagatag aagacaacaa cacacttgtg tteattgngg atgttaaage
                                                                        300
caacaagcac cagattaaac aggctgngaa gaagctgtat gacattgatg tggccaaggt
                                                                        360
caacaccctg attc
                                                                        374
<210> 765
<211> 288
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(288)
<223> n = A, T, C or G
<400> 765
aaatacaata attotgttat tgataaaatt taaggcattt toattgoott ttgcagattt
                                                                         60
actcataact acctaacaag gaaagaaggt ataattattt cagattggat tatttattct
                                                                        120
aaaattaaat tottoactaa tttattotaa gatgaattta atagtocato aggaaattgg
                                                                        180
nttttataaa gettatttta tgqqeataaa atacaqqaaa aqqtaataat aaatqeeaaa
                                                                        240
ccgtctcttt actttatgaa gccaaatatt tcctcagact tggttttt
                                                                        288
<210> 766
<211> 424
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(424)
<223> n = A, T, C or G
<400> 766
ttgtggttgt gcctgagggc tctgcttccg acactcatga acaggctatc ttgcggttgc
                                                                         60
aagtcaccaa tgttctqtct caqcctctqa ctcaqqccac tqttaaacta qaacatqcta
                                                                        120
aatctgttgc ttccagagcc actgtcctcc agaagacatc cttcacccct gtaggggatg
                                                                        180
tttttgaact aaatttcatg aacgtcaaat tttccagtgg ttattatgac ttccttgtcg
                                                                        240
aagttgaagg tgacaaccgg tatattgcaa ataccgtaga gctcagagtc aagatctcca
                                                                        300
ctgaagttgg catcacaaat gttgatcttt ccaccgngga taaggatcaq aqcattgcac
                                                                        360
ccaaaactac ccgggtgaca tacgcagcca aagccaaggg cacattcatc gcagacagcc
                                                                        420
acca
                                                                        424
```

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222

```
<210> 767
<211> 302
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(302)
<223> n = A, T, C or G
<400> 767
ggctttctca ataagcctca gctttctaag atctaacaag atagccaccg agatccttat
                                                                          60
cgaaactcat tttaggcaaa tatgagtttt attgtccgtt tacttgtttc agagtttgta
                                                                         120
ttgtgattat caattaccac accatctccc atgaagaaag ggaacggtga agtactaagc
                                                                         180
gctagaggaa gcagccaagt cgnttagtgg aagcatgatt ggtgcccagt tagcctctgc
                                                                         240
                                                                         300
aggatgtgga aacctccttc caggggaggt tcagtgaatt gtgtaggaga ggttgtctgt
                                                                         302
gg
<210> 768
<211> 94
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(94)
<223> n = A, T, C or G
<400> 768
ctgatctaaa agaagttact gaggaagatt tgaataatca ctttaagtct ttgggaagca
                                                                          60
gnnatttgaa atnttgaggt gacagncttt taag
                                                                          94
<210> 769
<211> 69
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(69)
<223> n = A, T, C or G
<400> 769
ctgcaagacg actccaaccc aacaacaacc. agatqngctn cagcccagcc ggncttcagt
                                                                          60
                                                                          69
tccatattt
<210> 770
<211> 222
<212> DNA
<213> Homo sapien
<400> 770
ctgaacgcaa accagccact ttaattaagc taagccctta ctagaccaat gggacttaaa
                                                                          60
cccacaaaca cttagttaac agctaagcac cctaatcaac tggcttcaat ctacttctcc
                                                                         120
cgccgccggg aaaaaaggcg ggagaagccc cggcaggttt gaagctgctt cttcgaattt
                                                                         180
```

gcaattcaat atgaaaatca cctcggagct ggtaaaaaga gg

```
<210> 771
 <211> 332
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(332)
 <223> n = A, T, C or G
 <400> 771
 ctgctttccc tcctatggct cccctggaac aggaggaga gccaaggggg cggcccagcc
                                                                          60
 tggacagege eegeteetge etgggtgeae acaeggeggg eetgagetee ageatetgag
                                                                         120
 tttgggggta tgagaacag gggagcagaa ggagaagaaa actgcctgtg ctgcaacacg
                                                                         180
 tttcctcatt tatttttct ttcttttct tttttctt tttttggaggg agaggtccct
                                                                         240
 gcaaggtccc ttcccgggca gnggagggat ggaaatgccg tcacagtagt agggactgga
                                                                         300
 gcgtctacaa ggatggaggg gagctactca gg
                                                                         332
 <210> 772
 <211> 194
 <212> DNA
 <213> Homo sapien
 <400> 772
 aaaagaaaga tcaattatat ccatgcttaa caggatcagc aggagcttta taaatgactt
                                                                         60
 tacagagact aataagggat ttgatctttc tttttttgtt atcgaggctt ttgaaatgtg
                                                                         120
 gaacttgtgt gttctgcttt atatgttata ttcaatatct tttcagatgc agtctatatt
                                                                         180
 ttatgctgag tttt
                                                                         194
 <210> 773
 <211> 272
 <212> DNA
 <213> Homo sapien
· <400> 773
 ccaattgatt tgatggtaag ggagggatcg ttgacctcgt ctgttatgta aaggatgcgt
                                                                         60
 agggatggga gggcgatgag gactaggatg atggcgggca ggatagttca gacggtttct
                                                                        120
atttcctgag cgtctgagat gttagtatta gttagttttg ttgtgagtgt taggaaaagg
                                                                        180
gcatacagga ctaggaagca gataaggaaa atgattatga gggcgtgatc atgaaaggtg
                                                                        240
 ataagctctt ctatgatagg ggaagtagcg tc
                                                                        272
 <210> 774
 <211> 314
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(314)
<223> n = A, T, C or G
<400> 774
gtgtcttgta cagttagnta tattagcagc cctctgagat gncgnatcta tcggaaggat
                                                                         60
ttcaaacace aattgcttta cctgaacaaa tggnncttac cctttgaaca gcanagngac
                                                                        120
cacgnagaag gaaggaaaag ggnaaaatcg cttnagttaa actgaaatta aatgaacaat
                                                                        180
aaggcaacta tataagtnac ttctagnagc attgcctgag anacaaatta ttgtttgata
                                                                        240
atttncattg tgaatagnaa tccaatagat catattgctt actttgntct ttttatacta
                                                                        300
tagaataata tttt
                                                                        314
```

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```
<210> 775
<211> 207
<212> DNA
<213> Homo sapien
<400> 775
cetgacagag etcageteae actgggaagt gtggatgeag ggtgeeette cetaececag
                                                                          60
tgagaaggaa gatteettae eeatettget teececcaag ggaagateat eatgeacgae
                                                                         120
ccatttgcca tgcggccctt ttttggctac aacttcgggc actacctgga acactggctq
                                                                         180
agcatggaag ggcgcaaggg ggcccag
                                                                         207
<210> 776
<211> 196
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(196)
<223> n = A, T, C or G
<400> 776
gtgaacggag gcactgtggc cgagaagctg gactggnccc gcgagaggct tgagcagcag
                                                                          60
gtacntgtga accaagtgtt tgggcaggat gagatgatcn acgtcatcgg ggtqaccaag
                                                                         120
ggcaaagnct acaaagggnn caccagtcgt tggcacacca agaagctgcc ccgcaagacc
                                                                         180
caccgaggac ctcggc
                                                                         196
<210> 777
<211> 325
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A, T, C or G
<400> 777
asagttgaac taagatteta tettggacaa ccagetatea ccaggetegg taggnttgte
                                                                          60
gcctctacct ataaatcttc ccactatttt qctacataqa cqqqtqtqct cttttaqctq
                                                                         120
ttettaggta getegtetgg tttegggggt ettagetttg geteteettg caaagttatt
                                                                         180
tctagttaat tcattatgca gaaggtatag gggttagncc ttgctatatt atgcttggnt
                                                                         240
ataatttttc atctttccct tgcggtacta tatctattgc gccaggtttc aatttctatc
                                                                         300
gcctatactt tatttgggta aatgg
                                                                         325
<210> 778
<211> 421
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(421)
<223> n = A, T, C \text{ or } G
<400> 778
ccaaaagaag taagacagct tgctgaagat ttcctgaaag actatattca tataaacatt
                                                                          60
```

```
ggtgcacttg aactgagtgc aaaccacaac attcttcaga ttgtggatgt gtgtcatgac
                                                                       120
gtagaaaagg atgaaaaact tattcgncta atggaagaga tcatgagtga gaaggagaat
                                                                       180
aaaaccattg nttttgtgga aaccaaaaga agatgtgatg agcttacnca nanaaatgag
                                                                       240
gagagatggg tggcctgcca tgggtatcca tggtqacaan aqtcaacaaq agcqtqactg
                                                                       300
ggttctaaat gaattcaaac atggaaaagc tcctattctg attgctacag atgtggcctc
                                                                       360
cagagngcta gatgtggaag atgngaaatt tgtcatcaat tatgactacc ctaactcctc
                                                                       420
                                                                       421
<210> 779
<211> 330
<212> DNA
<213> Homo sapien
<400> 779 '
ctgaactttc cgcttacgct gcccagagct gccaggtgta gactgagaat tcgagttttg
                                                                        60
tttcttcctt ggggttgtat ctgcagcctt ttctccctgg gactccctgt ctgctgccaa
                                                                       120
tggagttgaa gaactggaat gatgacacag ctcctcttct cttattttct ttgctqqcct
                                                                       180
ctccggtgtc tgggagcggg aggaggcttg ggctagagaa gggtgatgaa ctggggccat
                                                                       240
ttctcttcca gagctgtgag atgcctcgag tggagctgta ggaactggta atggcattgc
                                                                       300
ggctggagct agggatgcca cttgcgtaag
                                                                       330
<210> 780
<211> 279
<212> DNA
<213> Homo sapien
<400> 780
gagaggtaga gtttttttcg tgatagtggt tcactggata agtggcgttg gcttgccatg
                                                                        60
attgtgaggg gtaggagtca ggtagttagt attaggaggg gggttgttag ggggtcggag
                                                                       120
gaaaaggttg gggaacagct aaataggttg ttgttgattt ggttaaaaaa tagtagagg
                                                                       180
atgatgctaa taattaggct gtgggtggtt gtgttgattc aaattatgtg ttttttggaa
                                                                       240
agtcatgtca gtggtagtaa tataattgtt gggacgatt
                                                                       279
<210> 781
<211> 323
<212> DNA
<213> Homo sapien
<400> 781
ttgatcttct gcaggaaggt gcagcttttc catatcagct caaccacgcc gccagtccat
                                                                        60
tettaaggaa etgeegaeta ggaetgatga tgeattttag etttgagett ttgggggtta
                                                                       120
ttctaccaac aaacagtcca ttggaaagaa aacagtccct ggaattaaca gattagaatg
                                                                       180
ttcacactgg ttaatctttt tttaacaatg agcatgaagg tagcagaagc tggtgttt
                                                                       240
ccagatggtt cttctaacca aactaatttt tcactgttga caagcgaggc aagggttgca
                                                                       300
ctggaccaaa ggctgaggct tgg
                                                                       323
<210> 782
<211> 264
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(264)
<223> n = A,T,C or G
<400> 782
ttctagcttt gccctcactc cccggaaaaa ctgacactga cacaggngct ctttccttgc
                                                                        60
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226

ccctttagnt ggtacctcag tggggaggct tccttaccaa gaatgagttc ctgaaaccca 180 gggccagaga caaggacaac ttaggggaag acggggtttt cggtggagcc aggggcaaat 240 cttaatggga ccagnggggg ataccccaga gcccatggcc tgactgcaca gcctgcctgg 264 aggatgggtg cgcagttctg cnct <210> 783 <211> 159 <212> DNA <213> Homo sapien <400> 783 60 ctgtgtgaag gcgacagtgg tgcaggtctt cctgtggact agacgtccca gtcttgcctt 120 tcccttgata atgcagtaag ggacccccat tttacgacac agggcaggca agaagacaac cagctcgatg ggatccacgt cgtgtgcaat caccaccag 159 <210> 784 <211> 128 <212> DNA <213> Homo sapien <400> 784 ctcggccctc ttacaccatt ttgtttgatt gtctagtccc tgtttctttt tctttctaat 60 120 cettatteat ttaageaaaa ceatacatta tetttteeag teetttettg tattettaet gtttttt 128 <210> 785 <211> 346 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(346) <223> n = A, T, C or G<400> 785 ctgggctgat gctggaactc gtagaagtac acaggggccc gggaacactg aaaatgtgct' 60 120 acttggagtg cagggatcac aaacatggag tccgccatca tctcctggaa ctgcgcttgg agggtctggg gatccccatt gnccccaatg tactcctccc tcagcaggtc accaaatgta 180 ggaggcaaca tcagcagcgt taacattttc tgcagagcag cctgggaggc ctctctgtcc 240 atttccttct gggtatcata gatcctcatg accttgggga tgagccagcc gaattcattg 300 ttgttgacac caacaatgct agngnacagn ctgaaagtcg gcagag 346 <210> 786 <211> 118 <212> DNA <213> Homo sapien <400> 786 ctgcactgat ctgtggggag agttttacag acttttcatt ccagcctcct ccattgacag 60 tgaggtcttc attcaatcct gaagaaacct gaagtgtaga atctcctttt ccagattt 118 <210> 787 <211> 257 <212> DNA <213> Homo sapien <400> 787

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cactcattca tcgacctccc caccccatcc aacatctccg catgatgaaa cttcggctca
                                                                         60
ctccttggcg cctgcctgat cctccaaatc accacaggac tattcctagc catgcactac
                                                                        120
tcaccagacg cctcaaccgc cttttcatca atcgcccaca tcactcgaga cgtaaattat
                                                                        180
ggctgaatca tccgctacct tcacgccaat ggcgcctcaa tattctttat ctgcctcttc
                                                                        240
ctacacatcg ggcgagg
                                                                        257
<210> 788
<211> 155
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
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<223> n = A, T, C or G
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cgcaagagcc tatgnatgtg gnatccagaa ctcngtgngc gcaanccgca gagacccagt
                                                                         60
caccetggnt gtnetetatg ggccggacae ceceateatt tecceeceag actegtetta
                                                                        120
cctttcngga gcgaacctca acctctcctg ccact
                                                                        155
<210> 789
<211> 382
<212> DNA
<213> Homo sapien
<220>
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<222> (1) ... (382)
<223> n = A, T, C or G
<400> 789
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catggtttac cagattaatc tataaattca atacaaatcc aatcaaaatt tcaatgctct
                                                                        120
tgggtttgtt tgatttataa attgttggtc taattctaga agtaatatgg aggaacagtt
                                                                        180
ggctaagaat agccaagaca ctncaaggaa gaacaatttt gtggngatac tggagacaga
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ggtgaaattg gttacaatta tgacaaaatg tggaggcatc ttggttttta tcagaccttt
                                                                        300
toctaaagtt gcaataatca ggactgtact gtactgctac aagattagac aaattgatgt
                                                                        360
cagtcagaat agaaatcatc aa
                                                                        382
<210> 790
<211> 273
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1) ... (273)
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ggatccgcta cacagtttct gccagtccct gagttgatgc cttttcggct aactcgccag
                                                                         60
nttatcaatc tgatgttacc aatgaaagaa acggtnctta tgtacagnat catggtacac
                                                                        120
gcactccgnn ccttccgctc agaccctggc ctgctcacca acaccatgga tgtgtttgtc
                                                                        180
aagnagccct cctttgattg gaaaaatttt gaacanaaaa tgctgaaaaa aggagggtca
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tggattcaag aaataaatgt tgctgaaaaa aat
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<211> 344
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(344)
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agtcccatga aattaattat tttctctgct tgatcttggn ggacagtttc atgaagctgt
                                                                     180
caqttaqttc attaaagttt tggaaattct cagacagtgc agtggtatca gaaacttgta
ttcaaqaqta caqqtcaqaq ccttcttttc ttttcttttt gagatggagt cttgctctgt
                                                                     240
                                                                     300
tgccagactg gagtgcagtg gtgcgatctg ggctcactgc aatctccacc tcccgggttc
                                                                     344
aagcgattct cctgcctcag cctcccgagt aactgggact acag
<210> 792
<211> 227
<212> DNA
<213> Homo sapien
<220>
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<222> (1)...(227)
<223> n = A, T, C or G
<400> 792
                                                                      60
aagaagaaga agaagattaa ggaaaagtac atcgatnaag aagagctcaa caaaacaaaag
                                                                     120
                                                                     180
cccatctgga ccagaaatcc cgacgatatt actaatgagg agtacggaga attctataag
                                                                     227
agettgacca atgactggga agatcacttg gcagngaagc atttttc
<210> 793
<211> 328
<212> DNA
<213> Homo sapien
<400> 793
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aaacaagtca tttttcttga tcgttgtgga aggtttggag ccttagaggt atgtcagaaa
aaatatgttg gtattctccc ttgggtaggg ggaaatgacc tttttacaag agagtgaaat
                                                                     120
                                                                     180
ttaggtcagg gaaaagacca agggccagca ttgctacttt tgtgtgtgtg tgtgggtttt
                                                                     240
gttttgtttt tttggttggc cggttgtttt cgttgttgtt aacaaaggaa tgagaatatg
                                                                     300
taatacttaa ataaacatga ccacgaagaa tgctgttctg atttactaga gaatgttccc
                                                                     328
aatttgaatt tagggtgatt ttacctgc
<210> 794
<211> 290
<212> DNA
<213> Homo sapien
<400> 794
ccagcgagca catgaagcgg ttcttcatga actttgtggt tgggcaggat ccgggctcag
                                                                      60
acgccgcctt ccacttcaat ccgcggtttg acggctggga caaggtggtc ttcaacacgt
                                                                     120
tgcagggcgg gaagtggggc agcgaggaga ggaagaggag catgcccttc aaaaagggtg
                                                                     180
ccgcctttga gctggtcttc atagtcctgg ctgagcacta caaggtggtg gtaaatggaa
                                                                     240
atcccttcta tgagtacggg caccggcttc ccctacagat ggtcacccac
                                                                     290
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<210> <211> <212> <213>	343 DNA	sapien					
ctgag ctgcc ggtgt cttta	caaag accat aaata aaatt ataaa	aaatccttgt tgctttcatt aatttctgag cttttgaagt aattccacca ttgctgcatt	ttgaaaatga tcacagtctc ccttgccaag ttttcacttt	acttcaactc actaggaatg ataatcaatg tcttcgactc	cagaaagacc tgcaaatcaa gcatttacat acagcaagta	agtgtgtgct agcatatgtt ttgcttttt	60 120 180 240 300 343
<210><211><211><212><213>	354 DNA	sapien					
gggac attgc ggcag gtcca	ggccg tgata tgagg aggca tcctg	ctgaataagc gctcccaagg ctgtaagaac aagcaacaat cagcaaagac cctcagtgac	catcccccag taccctgggt ttctaatgat tttggtagac	cttgtgagta ccccgtggca ggggccacaa attgccaaat	acatcagtgc tggacaagct ttctgaaact cccaagatgc	ctgccaggtg tattgtagat tcttgatgtt tgaggtgggt	60 120 180 240 300 354
<210><211><212><212><213>	309 DNA	sapien					
cgttt tgggg agacg	ccgtc tggag tgggt tcccc atctg	tgcctgagcc tacggggcct cagagccgag cacccggaga tggtcccgat	tgagcgggtg ttaagagatt gacgtcgcgc	ggagctgtgt ttctttgttg tgtggcctga	gttgaagtac ctggacccct agtggcgcaa	agagggaggt tcttgaaggt gcttgctttg	60 120 180 240 300 309
<210> <211> <212> <213>	315 DNA	sapien	·				
caggo gctgt ccgcc	agcat agtct gtcag ccagg aaact	tgacgttctt gagtgtatcc ggtcaatctg caagattgac ctgtcccgtc agttg	taaacctatc atacttggct agcggtctcc	aggctggagt gctattccga aacttcttgt	tgttcacttt agcgcgtgtt tcactttctg	agccgagaag actgtttcct gtaaatggag	60 120 180 240 300 315
<210> <211> <212> <213>	157 DNA	sapien					
<400>	799						

ttcttccaaa	ctccatagtt tacctgtggc gggaaggggc	tcttgtccca	ctgcagccac			60 120 157
<210> 800 <211> 357 <212> DNA <213> Homo	sapien					
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<210> 801 <211> 359 <212> DNA <213> Homo	sapien					
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<210> 802 <211> 207 <212> DNA <213> Homo	sapien					·
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<210> 803 <211> 311 <212> DNA <213> Homo	sapien					
<220> <221> misc <222> (1) <223> n = R	(311)					
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<210> 804
<211> 202
<212> DNA
<213> Homo sapien
<400> 804
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tggctccgat tcgactctca gaccaagagc atcttcgagc aagaaactaa taataataat
                                                                        120
tccagcttct acacaggagt ctatattctg atcggagccg gcgccctcat gatgctggtg
                                                                        180
ggcttcctgg gctgctgcgg gg
                                                                        202
<210> 805
<211> 238
<212> DNA
<213> Homo sapien
<400> 805
ccaaccagtc tggctggagt gatgcattcc tggcccagca cacgatgctt accctggatc
                                                                         60
ecaacgtcac eggtgtette etgggaceet acceetttgg categateet atttggagee
                                                                        120
tggctgccaa ccacttgagc ttcctcaact ccttcaagat gaagatgtcc gtcatcctgg
                                                                        180
gcgtcgtgca catggccttt ggggtggtcc tcggagtctt caaccacgtg cactttgg
                                                                        238
<210> 806
<211> 325
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A, T, C or G
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                                                                         60
ccacgccgag gccggcaaca aacgacagta tctcggattc ctttttttt taattttta
                                                                        120
tactttggng tttcacttcg ngctctgaat actgaataac catgaatgac tgaatagttt
                                                                        180
agtccagatt tttacagagg atacatctat ttttatcatt atttggggtt tgaaaaattt
                                                                        240
ttttttacac cttctaattt ctttatttct caaagcagat aattcttctg ngtgaaaatg
                                                                        300
ttttctttt ttaatttaag gttta
                                                                        325
<210> 807
<211> 289
<212> DNA
<213> Homo sapien
<400> 807
cctaaaggga actgtcttct gtcgagaagt aaaggaaact tcatgaagga tgtagaagct
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tagctgcctc agagaagaga gaacctgaag atctgaggca agctggacag gagaggtaga
                                                                       120
tatttgttga tggaagaatt caagtttata atcaattccc acttagcacc tactgtgtgc
                                                                       180
taggaacttg aatgtgtatg tttgacaagt cctgcttggc ctgatgggtg ggagaaggaa
                                                                       240
cctgagcctg gctgagatgg ctaggcggag ggctttgaag tccaagcag
                                                                       289
<210> 808
<211> 376
<212> DNA
<213> Homo sapien
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aaaaaaaact gcacatgtta atataagtaa ccatcaaagc	gtgcagtatg ttataaatta cagaacaaaa tcattctggg ctaatgaaag	tacccctca gaaaatggaa acaacaggat ggtagtcaag	cgaaatttag gagaagtaga aatgtatccc gagggagtgg	tgtcataagc tttggcaggg aataaatcca ccccaaaggc agggagaaaa gaaaaaaggt	aaaacaagat tgagtattat ccagtagaga agaacgcaga	60 120 180 240 300 360
<210> 809 <211> 243 <212> DNA <213> Homo	•					0,0
<220> <221> misc <222> (1) <223> n = 1	(243)					
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<210> 810 <211> 274 <212> DNA <213> Homo	sapien					
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<210> 811 <211> 205 <212> DNA <213> Homo	sapien					
cccaactaca aaatctcgaa	cggagttcaa	gttccctcag ggccatcgcg	attaaagctc	aacaaatccg acccctggac gcctgctgga	aaaggtgttc	60 120 180 205
<210> 812 <211> 199 <212> DNA <213> Homo	sapien					
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tttgggaaag	aatgatttt					199
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<220> <221> misc <222> (1). <223> n = 1	(334)					
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<210> 814 <211> 358 <212> DNA <213> Homo	sapien					
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<210> 815 <211> 203 <212> DNA <213> Homo	sapien					
ggacgtgtac	agacgctccc ttctacctgg	acaagcctct ccttcgagaa	ctaccagagc gcccaagggg ctccttgcac	accatgatgg	agacgctgtc	60 120 180 203
<210> 816 <211> 92 <212> DNA <213> Homo	sapien					
<400> 816 cggccgcaga gcacacgttg	agcgagatga tgccgccgct	cgaagggaac gtggctctaa	gtcatcgttt gg	ggaaagcgtc	gcaataagac	60 92
<210> 817 <211> 367 <212> DNA <213> Homo	sapien					

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ttaatacttc tataagagaa aaaacagtgg ggaatggaaa	atttgaattt cttactttac agaatgtatt caactctgtg aaataccaga tttactattt	tatctttctt gaaagaagcc ggatggacat agatggacca	ctctacctta tactctcata gcagccgttt gcacttataa	ctattatttt atttatggga ggcatggtta ttttttatca	cttacacatt tggtgcaagg tgaagttcat tggagctatt	60 120 180 240 300 360 367
<210> 818 <211> 381 <212> DNA <213> Homo	sapien					•
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<210> 819 <211> 109 <212> DNA <213> Homo	sapien					
ccgaattgca	ttccagacca aaggaagaag				tgaagaaaga	60 109
<210> 820 <211> 309 <212> DNA <213> Homo	sapien					
<220> <221> misc <222> (1). <223> n = 1	(309)					
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<210> 821 <211> 236 <212> DNA <213> Homo	sapien		·			
	ctgaatgctg gaagagagag					60 120

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agtggcggaa aagctagaag ctctctcggt gaaggaggag accaaggagg atgctgagga
                                                                      180
 236
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<211> 388
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(388)
<223> n = A, T, C \text{ or } G
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                                                                      60
cggcggtctc cgaggctatc tacgggtttt tttcaggaca aatgatgcga aggttgntac
                                                                     120
attagtgggg gaagacaaat atggaaacaa atactatgaa gacaacaagc aattttttgg
                                                                     180
ccgtcaccga tgggttgtat atactactga aatgaatggc aaaaacacat tctgggatgt
                                                                      240
ggatggaagc atggtgcctc ctgaatggca tcgttggctt cacagtatga ctgatgatcc
                                                                     300
tccaacaaca aaaccactta ctgctcgtaa attcatttgg acgaaccata aattcaacgn
                                                                     360
gactggcacc ccagaacaat atgtacct
                                                                     388
<210> 823
<211> 353
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(353)
<223> n = A,T,C or G
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tgcaaaacga aaaatgaagc agctacatgt agttagtaat ttctagtttg aactgtaatt
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gaatattgtg gcttcatatg tattatttta tattgtactt ttttcattat tgatggnttg
                                                                     180
gactttaata agagaaattc catagttttt aatatcccag aagtgagaca atttgaacag
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tgtattctag aaaacaatac actaactgaa cagaagtgaa tgcttatata tattatnata
                                                                     300
gccttaaacc tttttcctct aatgccttaa ctgtcaaata attataacct ttt
                                                                     353
<210> 824
<211> 264
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G
<400> 824
ctgggtgcag gcgggctgag tccgaaaaga gagtcagcaa agggagatgg ggtggggccg
                                                                      60
ttttatagga ttagggaagg taatggaaaa ttacagtcaa agggggtttg ttctctggtg
                                                                     120
ggcaggtgtg gatctcacaa agtacactct caagggtggg gagaattaca aaggaccttc
                                                                     180
ttaagngtgg gggagattac aaagtacatt tatcagttag ggnggngcag gaacaaatca
                                                                     240
caatgttgna atgtcatcag ttaa
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<211> 361
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(361)
<223> n = A, T, C or G
<400> 825
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                                                                         60
ggcatgatct ccccaatgtg tttttactcc ttttccggct tctaggacag aggtatgtag
                                                                        120
tcaaagaatc ctatggtgga tctgaattgg gtttcagcta ctgtacctgg tccttgtgaa
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ttaaaaaaat aaagtcacaa aaaccatatn acaaaacaaa ttaaaataaa tagacaaaat
                                                                        240
                                                                        300
gaagetgtet ccagacette tgcattgaca cacaggtttg aagteaacea aageacteat
getaatctgg atgggaacac tagggagaca gaaaccccag tatgaaacca tgtacttgag
                                                                        360
                                                                        361
<210> 826
<211> 195
<212> DNA
<213> Homo sapien
<220> .
<221> misc_feature
<222> (1)...(195)
<223> n = A, T, C or G
<400> 826
                                                                         60
ccccagaagn gacgcagccc tctatnggcc cnaatcttct tcantcgctc caggtcttca
cggagettgt tgtccagacc attggctagg acctggctgt attttccatc ctttacatcc
                                                                        120
ttctgtctgt tcaagaacca gtctgggatc ttgtactggc gnggattctg cataatggng
                                                                        180
                                                                        195
atcacacgtt ccacc
<210> 827
<211> 227
<212> DNA
<213> Homo sapien
<400> 827
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244

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gggccgctgc gggctccggg ggggtcccgg gatggtggag ggcagctgcg agagtgacac	ggggccgggg	tcggggcctg			120 180 215
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 gaagctcacg gncgacacga ggctgcgcag gatctggctt gcttccgact cgctgaagtg
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 ccgcntcttg cggatgtgct ccagcagctc cccgccccgc agcagctcca ggaccaggta
                                                                        240
 cgtgtgcagc tggtcgtgat gcacctcgtg cagattcacc acgttggggt gtgactggca
                                                                        300
caggegeagg geageeactt egegetgegt gttegeetee ageetgegae tgaggatett
                                                                        360
 gactgcgaac tcctggccgc tctggcgctg gcggcagcgg cgacacacag aaaagctgcc
                                                                        420
 ctggcccagc gcaggctccc gcaggtccag ctcgtactgc tggaagaagg gcgagtcctg
                                                                        480
 catcatagcg ctcctggcca ccg
                                                                        503
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<213> Homo sapien
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cgcgtcgacg cggccgcg
                                                                         78
<210> 880
<211> 211
<212> DNA
<213> Homo sapien
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                                                                         60
atagtcctgt ggtgatttgg aggatcaggc aggcgccaag gagtgagccg aagtttcatc
                                                                        120
atgcggagat gttggatggg gtggggaggt cgatgaatga gtggttaatt aattttatta
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gggggttaat tttgcggtcg acgcggccgc g
                                                                        211
<210> 881
<211> 373
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(373)
<223> n = A, T, C or G
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                                                                         60
caccegegea gtggaacgag aggeegtnga agagegagae etgeeaggge tgegageege
                                                                        120
gcgcgcacgg ggcgccatag gcttcggggt ccaagcgcgt gtcgttttgg gggagcagcg
                                                                        180
ccgcctctgc ggcccagagt tgcgccatca gcagcggcag cagcttcgcc agagcccggg
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cgccagaggc ggcggagagg tggaggtgcg gagctctcat ggccaggatc tgggagtcgc
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cgataggaag gagggagggg acccagacgt gcctntgccc tgcctgtggt ctgccgcgtc
                                                                        360
cgacacggcc gcg
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<210> 882
<211> 300
<212> DNA
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<221> misc_feature
<222> (1)...(300)
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<223> n = A, T, C or G
. <400> 882
                                                                          60
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tagettecae tttettteat gaaactgagg teaggeaaga aacaaaaate caecaagtee
                                                                        180
tetecateet gecatggegt cetggeetgt gaggacatgg ggegeetggg agegggggg
gaggetggge ageactggge cagaggegte etggteactg etceacetgg teactgetee
                                                                        240
acctcatgct gagaggagcc tgtgtgtcaa accccagggg aaaaaagggac aggcagatcg
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<210> 883
<211> 230
<212> DNA
<213> Homo sapien
<400> 883
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gggccgctgc gggctccgqg agagggtcga aggtgaagat ctcaggaccg gagccccgcc
                                                                        180
ggggtcccgg gatggtggag ggggccgggg tcggggcctg caggatggtc atggtcgggt
                                                                        230
ggcagctgcg agagtgacac atggtgagcc gagcggtcga cgcggccgcg
<210> 884
<211> 601
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(601)
<223> n = A, T, C or G
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                                                                         60
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aagctgattg aagcaaccct ctactttttg gtcgtgagcc ttttgcttgg tgcaggtttc
                                                                        120
attggctgtg ttggtgacgt tgtcattgca acagaatggg ggaaaggcac tgttctcttt
                                                                        180
                                                                        240
gaagtagggt gagtcctcaa aatccgtata gttggtgaag ccacagcact tgagcccttt
                                                                        300
catggtggtg ttccacactt gagtgaagtc ttcctgggaa ccataatctt tcttgatggc
                                                                        360
aggeactace ageaacgtea ggaagtgete agecattgtg gtgtacacea aggegaceae
                                                                        420
agcagctgca acctcagcaa tgaagatgag gaggaggatg aagaagaacg tcacgagggc
                                                                        480
acacttgctc tcagtcttag caccatagca gcccaggaaa ccaagagcaa agaccacaac
                                                                        540
gccggctgcg atgaggaagt agcccacgtt gacaaactgc atggcactgg acgacagtgg
                                                                        600
cccgaagatc ttcanaaagg atgccccatc gattgacacc cagatgccca ctgccaacag
                                                                        601
<210> 885
<211> 207
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(207)
<223> n = A, T, C or G
<400> 885
                                                                         60
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ttgtggccct tgagggtgcc annaagggtc atctgctcag ncatggcggc ggcgagagcg
                                                                        120
                                                                        180
tgtgtcnntg cagcgacgag gatggcactg gatggcttag agaaactagc accacaacct
                                                                        207
ctcctgccgc cggtcgacgc ggccgcg,
```

```
<210> 886
<211> 442
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(442)
<223> n = A,T,C or G
<400> 886
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                                                                         60
agtcacccca cggctatggg gaaattancc cgaggcttag ctttcattat cactgtctcc
                                                                        120
cnnggtgtgc ttgtcaaaga gatattccgc cnagccanat tcgggcgctc ccatcttgcg
                                                                        180
caagttggtc acgtggtcac ccaattcttt gatggctttc acctgctcat tcaggtaatg
                                                                        240
tgtctcaatg aagtcacaca aatgggggtc atttttgtca gnggccagtt tgtgcagttc
                                                                        300
cagtagtgac tgattcacat ttttttccaa atgtaatgca cactccattg cattcagccc
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gctctcccag tcatcacagt ctggtttntt gatatcctga aggaagattc ggccacctcg
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tnggttctgc agcttcatca gt
                                                                        442
<210> 887
<211> 222
<212> DNA
<213> Homo sapien
<400> 887
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gcgccaggac cacctcggcc gtcaccttag ccaggtggct gcttaggtcc actgtgcgct
                                                                        120
tcacgtcctc attgatcagc ggcggtgcct cggaggaggc gctgcccggc gccggggccc
                                                                        180
aagtcccaag caacaggagc agaaacaagc cggcggctgg cg
                                                                        222
<210> 888
<211> 89
<212> DNA
<213> Homo sapien
<400> 888
ggtggcgtag cgcccgctta taaagccgca acaccttttg ctgatgggtc aggtagggtc
                                                                         60
ccgacgccaa gaacgccatt acggccgcg
                                                                         89
<210> 889
<211> 451
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(451)
<223> n = A,T,C \text{ or } G
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                                                                         60
gctgctccgg gcccaacacc agccctggcc aggctctccc ctcccagggg cagcgcccag
                                                                        120
tecceagggg etgecagage cetgtgtgee ttgeegeatt eccetgatge agettttgge
                                                                        180
aactgaaagg cagggctctc gctgagtgca cctggggctt cctgagccca tctgcggcgg
                                                                        240
ccccaccctg gcctaggtgc tgagtgcagc tgctgcagac agcccctccc tccttagtgg
                                                                        300
agcctggagg gtggggtgct cggggatgca ggcaggggca ggggctccag agccacaggt
                                                                        360
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cagaagcagg gctgggggag gactaggggc agggacagaa			aggcaccctc	acagctaggt	420 451
<210> 890 <211> 66 <212> DNA <213> Homo sapien					
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<210> 891 <211> 599 <212> DNA <213> Homo sapien					·
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<210> 892 <211> 113 <212> DNA <213> Homo sapien					
<400> 892 gtctcaaaca ggaccgcatt gccagcaagt cattcatggt	, , ,				60 113
<210> 893 <211> 208 <212> DNA <213> Homo sapien					
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<210> 894
 <211> 67
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc feature
 <222> (1)...(67)
 <223> n = A, T, C or G
 <400> 894
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                                                                      60
                                                                      67
 <210> 895
 <211> 58
 <212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(58)
<223> n = A, T, C or G
<400> 895
58
<210> 896
<211> 177
<212> DNA
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<221> misc_feature
<222> (1)...(177)
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ctnagtgagt ataaatacgc caanaanagc tgtggcttct ttcactggtg tcctcagaaa
                                                                     120
ggctgtgagc agtgttggtg gcatacctgt cacagcatct agcaaagcac ctgaatt
                                                                     177
<210> 897
<211> 542
<212> DNA
<213> Homo sapien
<400> 897
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aggatgagtt tggagcggta ctccttcagc cgctgcacgt tggtctgcag ggactccgtg
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gacttgttcc gcctcctcgg atccacagaa atgccgatgg tccgggccac cttcttgtga
                                                                     240
atgeoggeca cectgagete etccaggetg aageogegge eggegegeae ettegtgtgg
                                                                    300
taccgaaccg tggggcagcg cacgatgggc cggatgggac ccgacgcggg gcgcgggggg
                                                                    360
atgcggcgcg cettggcttg ccgggcctta cgtctgcgga tcttacgggc cggctggttg
                                                                     420
aaccacgtgg ccacgcgccg ctgccagtcc ttgtggaagt ggggcttcaa gaccatgcca
                                                                     480
ttccggctgg gcgccatggc tgcctacggc cctgcggctc ctggtcgacg cggccgcgaa
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. 254

tt						. 542
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<220> <221> misc <222> (1). <223> n = 1	(165)					
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<210> 899 <211> 67 <212> DNA <213> Homo	sapien				÷	
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<210> 900 <211> 77 <212> DNA · <213> Homo						
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<210> 901 <211> 114 <212> DNA <213> Homo	sapien					
	ggacggctgg gatgacgata					60 114
<210> 902 <211> 64 <212> DNA <213> Homo	sapien .		·			
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<210> 903 <211> 63 <212> DNA <213> Homo	sapien					

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                                                                         63
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<211> 142
<212> DNA
<213> Homo sapien
<400> 904
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                                                                         60
gagacagaag acggcattgt cgattcactg tcccaggtca ggtcgacgcg gccgcgaatt
                                                                        120
ccaccacact ggactagtgg at
                                                                        142
<210> 905
<211> 101
<212> DNA
<213> Homo sapien
<400> 905
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                                                                         60
tgtgatggcg tcacagaaga gaccctccca gaggcacgga t
                                                                        101
<210> 906
<211> 506
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(506)
<223> n = A, T, C or G
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                                                                         60
gtcaacaatt tacggagggt ccagccgctg ggtcagattg agacaaacca ttgtgtggtt
                                                                        120
gggtttgggt cagcaggctg gagagggttc tgttcttttt gatcattatc gtttgggcc
                                                                        180
ccaagggagg gtcttgggag ccacctgagc cccaaagctg ggaaattcct canagctgct
                                                                        240
catgtcagga gccttctcac tgctgctggc ggnccagggt gcgtcccgca ccacaaagcc
                                                                        300
tntggaaggt gccttggcct cttcgtgtgc tgggggtttc atgtatacct gcagcgcctc
                                                                        360
actgtccacc acgtcagcta ggtattcctc ctccagattg aggatgtggt cgatggcttc
                                                                        420
etecacatte tetgggagee cegteacagt gacgeagttg gggtetgggg etecgetetg
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tgggaagcga atgtccacct tgaatt
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<211> 93
<212> DNA
<213> Homo sapien
<400> 907
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aggacctgat tgccaaaggc cccgtctcaa agt
                                                                         93
<210> 908
<211> 238
<212> DNA
<213> Homo sapien
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<210> 910 <211> 93 <212> DNA <213> Homo	sapien					
	caagttcacg tgccaaaggc			ggaggttggg	ggctctgtgg	60 93
<210> 911 <211> 261 <212> DNA <213> Homo	sapien					
ctcgcaggtg gatgtgggcc tgaggcaaac	gggctgaaga acattcttca tctgtgccgg attttgtaca acgcgggaat	tggggtccag tgcagtccat ctttggtatt	tgacacctgg ggagaatggc	gggcccagct cagtagcgct	tgcagctgga gcttcctccg	60 120 180 240 261
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266

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cccacccagc ccagcaggc catggagaag cccagcaact gcaggcccga attggccatt
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                                                                        300
tecgecetea gaaaacaetg ggggegeegg gegggagaee etacagtaaa acaaacgaea
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caaaaagggt ttgggccagg tgaatgcaaa tcttgtcacc aaactacaca caaatcgacc
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cctccagtga agcgatggcc tcgcggcaca gggagtagga tacgccggga gggtggttcc
                                                                        480
agacaaaatt ggtggtcccc gaaggccagg cggttccctc cgggcgctct cggcgaccct
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gggcctctga caacaagcca ccgctcgtgc gctcctgtag ccgcacgtct tccaqqaact
ggtcaacctc cagccccagc ggctcctqag caaqccgccg ccagccccqc ttcttatttc
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ttgggcctcg ccgccgccgc ctcagcgctg ggtccaccga agtgggccgc agccccagga
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aaccagaatc ggcatcgctt ttcgagctgc gcttcccacc aacgccactg cctgtcgacg
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cggccgcgaa tt
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<210> 957 <211> 62 <212> DNA <213> Homo	sapien			·		
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attcaagatc ctgatggcta ctggattgaa attttgaatc ctaacaaaat ggcaacctta
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ggctgtgagc agtgttggtg gcatacctgt cacagcatct agcaaagcac ctgaatt
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ctggtggccg gttgttgaag gtcattgcag agaggaagga agccgaggag gggagcctgc
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agtgagggcg tcctggggtt ctncggttct caccaccctt gggccacgcc gtctagtcca
                                                                        240
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cacctgagga gttggtcagg tagaaggggc ggatgaccqt gcggaagccg ttgaantgcc
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                                                                        360
tegeageett ccageeeteg aaateggtga egtetgeeae gaagageeet tegeagagea
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tcagggettt gttttegtag geaatggtge gatetgagee gecagaettg gtgaggeeea
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ggacagggag
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<211> 159
<212> DNA
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 <223> n = A, T, C or G
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 ggagcgggcg ggggccggac gtcgacgcgg ccgcqaatt
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 <212> DNA
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                                                                        120
 cggggtcccg ggatggtgga gggggccggg gtcggggcct gcaggatggt catggtcggg
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tggcagctgc gagagtgaca catggtgagc cgagcgt
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<212> DNA
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                                                                        120
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tecgecetea gaaaacaetg ggggegeegg gegggagaee etacagtaaa acaaacgaea
                                                                        300
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caaaaagggt ttgggccagg tgaatgcaaa tcttgtcacc aaactacaca caaatcgacc
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cctccagtga agcgatggcc tcgcggcaca gggagtagga tacgccggga gggtggttcc
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<212> DNA
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geogeotetg eggeocagag ttgegocate ageageggea geagettege cagageegg
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ccgatangaa ggagggaggg g
                                                                        321
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<212> DNA
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gagtggagag tactggattg accccaacca aggctgcaac ctggatgcca tcaaagtctt
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ctgcaacatg gagactggtg agacctgcgt gtaccccact cagcccagtg tggcccanaa
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ccagctgacc ttcctgcgcc tgatgtccac cgaggcctcc cagaacatca cctaccactg
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caagaacagc gtggcctaca tggaccagca gactggcaac ctcaagaagg ccctgctcct
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                                                                        540
ecagggetee aacgagateg agateegege egagggeaac ageegettea eetacagegt
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<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(650)
<223> n = A, T, C or G
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gagtggagag tactggattg accccaacca aggctgcaac ctggatgcca tcaaagtctt
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ccagctgacc ttcctgcgcc tgatgtccac cgaggcctcc cagaacatca cctaccactg
                                                                        420
caagaacagc gtggcctaca tggaccagca gactggcaac ctcaagaagg ccctgctcct
                                                                        480
ccagggetec aacgagateg agateegege egagggeaac ageegettea ectacagegt
                                                                       540
cactgtcgat ggctgcacga gtcacaccgg nagcctgggg caagacagtg attgaataca
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<210> 968
<211> 629
<212> DNA
<213> Homo sapien
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<220>

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<221> misc feature
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 <223> n = A,T,C or G
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                                                                         120
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                                                                         420
 caagaacage gtggcctaca tggaccagca gactggcaac ctcaagaagg ccctgctcct
                                                                         480
 ccagggctcc aacgagatcg agatccgcgc cgagggcaac agccgcttca cctacagcgt
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                                                                         600
 aaaccaccaa gacctcccgc ctgcccatc
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 <211> 222
 <212> DNA
 <213> Homo sapien
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 catccatgct ccacgggttc ttgggagtga ccgggatggg aatcccgtgt tgctttgcgt
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acggacggga agcaacgga
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<213> Homo sapien
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<210> 972
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<212> DNA
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<220>
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<210> 974 <211> 180 <212> DNA <213> Homo sapien				•	
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<211> 66
<212> DNA
<213> Homo sapien
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                                                                         66
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<211> 114
<212> DNA
<213> Homo sapien
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                                                                        114
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<211> 177
<212> DNA
<213> Homo sapien
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ggctgtgagc agtgttggtg gcatacctgt cacagcatct agcaaagcac ctgaatt
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<212> DNA
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<221> misc feature
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ggaggcaggc gggccgaacc aggcggagat cctagaagga gcggagaagg tcgacgcggc
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cgcgaatt
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<210> 981
<211> 184
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(184)
<223> n = A, T, C or G
<400> 981
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agagccccag accgggcggc tttgcactga tgagctgcag ggcaggtcga cgcggccgcg
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aatt
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<210> 982
<211> 98
<212> DNA
<213> Homo sapien
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cccgacccgc gggcgaggcc gggtacctgg gctgggat
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<210> 983
<211> 425
<212> DNA
<213> Homo sapien
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<221> misc feature
<222> (1)...(425)
<223> n = A, T, C or G
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                                                                         120
cggcctggcc cagggcggga gtgccggctg gggcgcgctg ctcttcacgc tctctgatgg
egtgetggee tgggacacet tegeceagee cetgeeceat geceneetgg tgateatgae
                                                                         180
cacctactat gctgcccagc tcctcatcac actgtcagcc ctcaggagcc cggtgcccaa
                                                                         240
                                                                         300
gactgactga ctagggaget tgaagggeeg gtgtteagge ceteteetee tgeaaggaee
                                                                         360
tgggcctccc agcccagccc agcctgagaa ataccctcag cagcgaagct tcctgacgcc
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gaatt
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<210> 984
<211> 148
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(148)
<223> n = A, T, C or G
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                                                                          60
                                                                         120
gagacagaag acggcattgt cgattcactg teccaggtca gtggtgggtc gacgeggccg
                                                                         148
cgaattccac cacactggac tagtggat
<210> 985
<211> 461
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(461)
<223> n = A, T, C or G
<400> 985
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<210> 986 <211> 138 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(138) <223> n = A,T,C or G	
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<210> 987 <211> 555 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(555) <223> n = A,T,C or G	
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<210> 988 <211> 318 <212> DNA <213> Homo sapien	
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<210> 989
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<212> DNA
<213> Homo sapien
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                                                                        120
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gagtggagag tactggattg accccaacca aggctgcaac ctggatgcca tcaaagtctt
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etgcaacatg gagactggtg agacctgcgt gtaccccact cagcccagtg tggcccagaa
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gaccgatgga ttccagttcg agtatggcgg ccagggctcc gaccctgccg atgtggccat
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ecagetgace ttectgegee tgatgtecae egaggeetee cagaacatea cetaceaetg
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caagaacage gtggcetaca tggaccagea gactggcaac etcaagaagg eectgeteet
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etecttetgt gegeagtttg tagtagttet taeactggta gegaacegag tgeteeacat
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tgagacetge gtgtacecca etcageccag tgtggeccag aagaactggt acateageaa
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catggaccag cagactggca acctcaagaa ggccctgctc ctccagggct ccaacgagat
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cctgcccatc atcgatgtgg cc
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tgtaagtetg gtttttttat etgtaagata attgtgtg
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gagagcgtgt gtcgctgcag cgacgaggat ggcactggat ggcttagaga aactagcacc
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agtggagagt actggattga ccccaaccaa ggctgcaacc tggatgccat caaaqtcttc
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tgcaacatgg agactggtga gacctgcgtg taccccactc agcccagtgt ggcccagaag
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	•••				
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aagatgacct acgggctcct acaacatttt tataagcaac tgagagaaga ttcctctcct
                                                                       120
cattggataa ttcagctcct tgctcagtta cagacttcat gcaggctgcc atgtcatcat
                                                                       180
                                                                       240
ategeteage etgeteggee agtttggeet tetgaaceag eteattttta tecatgaetg
                                                                       300
gatgttctgt gtccggagtg ggtggtggcg gcggacggac gggctcagca gtctctgggc
                                                                       355
ggeggeggeg geageagegg egaggetgag actetytece gtegaegegg eegeg
<210> 1027
<211> 148
<212> DNA
<213> Homo sapien
<400> 1027
                                                                        60
tgccaccetg gtgcccatga ctgtggcctt ggtgcccagg aggggccaga gctggtgggt
                                                                       120
getggetgtt etteteete tggeeetgag eecetggete tggagetgee tgtagggget
                                                                       148
gaagggccat cccactgcca ttctccgg
<210> 1028
<211> 479
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A, T, C or G
<400> 1028
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                                                                       120
ctagtggaag ccttccagta atttcttgaa gctgagcgct caggtgagta gggcgacatc
tggtggccgg ttgttgaagg tcattgcaga gaggaaggaa gccgaggagg ggagcctgca
                                                                       180
                                                                       240
gtgagggcgt cctggggttc tccggttctc accacccttg ggccacgccg tctagtccac
                                                                       300
acctgaggag ttggtcaggt agaaggggcg gatgaccgtg cggaagccgt tgaagtgccc
                                                                       360
tgccgggcag gggaaggagg aggtgctctt cgagctgttg gtgtccaggg cactgggaat
                                                                       420
cgcagccttc cagccctcga aatcggtgac gtctgccacg aagagccctt cgcagagcat
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```

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<211> 64
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(64)
<223> n = A, T, C or G
<400> 1029
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                                                                         60
tggg
                                                                         64
<210> 1030
<211> 531
<212> DNA
<213> Homo sapien
<400> 1030
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gtgccaacag gatgacatga aatgatgtac tcagaagtgt cctggaatgg ggcccatgag
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atggttgtct gagagagagc ttcttgtcct acattcggcg ggtatggtct tggcctatgc
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cttatggggg tggccgttgt gggcggtgtg gtccgcctaa aaccatgttc ctcaaagatc
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atttgttgcc caacactggg ttgctgacca gaagtgccag gaagctgaat accatttcca
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gtgtcatacc cagggtgggt gacgaaaggg gtcttttgaa ctgtggaagg aacatccaag
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atetetggte catgaagatt ggggtgtgga agggttacca gttggggaag etegtetgte
                                                                        420
tttttccttc caatcagggg ctcgctcttc tgattattct tcagggcaat gacataaatt
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gtatattcgg ttcccggttc caggccagta atagtagcct ctgtgacacc a
                                                                        531
<210> 1031
<211> 518
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(518)
<223> n = A, T, C or G
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tgcctgagca gtcggctgtg actctcgaca atgtaactct gcaaatcgat ggagtccttt
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acctgcgcat catggaccet tacaaggcaa gctacggtgt ggaggaccet gagtatgccq
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tcacccagct agctcaaaca accatgagat cagagctcgg caaactctct ctggacaaag
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tetteeggga acgggagtee etgaatgeea geattgtgga tgeeateaac eaagetgetg
                                                                        360
actgctgggg tatccgctgc ctccgttatg agatcaagga tatccatgtg ccacccggg
                                                                        420
tgaaagagtc tatgcagatg cangtggagg cagagcggcg gaaacgggcc acagttctag
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agtctgaggg gacccgagag tcggccatca atgtggca
                                                                        518
<210> 1032
<211> 116
<212> DNA
<213> Homo sapien
<400> 1032
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                                                                         60
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tcaccctgat cagaggattg agtaaacggc taggctagag gtggctagaa taaataggag	240 241
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trytgrgeet gerggagtae ceeeggggga agaggaagaa gggeteeace atggaggget	60 120
ggggacagaa gcacatgacc gccgtggtga agctgttcgg gccctttacc aggaattact atgttcgggc cgtcctgcat ctcctgctct cggtgcccgc cggcttcctg ctgg	180 234
<210> 1035 <211> 434	
<212> DNA	
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<222> (1)(434) <223> n = A,T,C or G	
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additigitg teathinite aaagaatega naattgegta caaagaaaac cttacataaa	180
ttaanaatga atacatttac aggcgtaaat gcaaaccgnt tccaactnaa agcaagtaac agccacggn gttntggcca aagacatnag ntaanaaagg aaactgggtc ctacggcttg	240 300
gactttncaa ccctgacaga cccgcaagac aaaacaactg gttnttgcca gcctntanag aaatcccana acactnagcc ctgacacgtt aataccctgc acanatcana ggctgntggc	360 420
cacacanact cacc	434
<210> 1036 <211> 294	
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gcctccacag ccttggctca gtgtccctgt gtacaagacc cagtgacttc caggctccca gaaaccccac cctaaccatg ggccaaccca gaacacccca ctctccacca ctgg	180 240
- gadacacca Ctcccacca ctgg	294

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<211> 547
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(547)
\langle 223 \rangle n = A, T, C or G
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catgaaaaca aatggtctgt aatcttataa accaacatag catttcactg tcaacaatgt
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                                                                        240
gaaaatttaa tatcttctca aacaggcata agatgaagaa gtgctatttt ttaattgtaa
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aaggaactta tgtaatgnta aaattacatt ataatttttc attccqaatt gacaaatgat
ttcaaaaaca aggnatcaaa gtttgactgc aaatagtaat gcaatataat ttcataaaaa
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tccttcaatt tctatttttt tccttttctq tagttgacat atgaagacca cttcaatttc
                                                                        420
                                                                        480
taaaaaaggg aaccattcca attttccctc cccaagaaaa tgtctcacaa ttacaaagta
qaaaaacagc cgttcataaa atgcaaaaaa aanttctgat tttatacatg aaataatttc
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                                                                        547
tagatca
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<211> 451
<212> DNA
<213> Homo sapien
<400> 1038
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qaataqtqtq tqtaqcqaca ctaqtqaaaq caqtqctqct qaatttqatq ataqqcqggq
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agttttgagg agtatcagct gcgaagaagc cacttgcagt gacaccagtg agagcatttt
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qqaaqaqqaa ccacaaqaaa atcaaaaqaa acttttqccc ttatcaqtaa cacctqaqqc
                                                                        300
                                                                        360
tttttctgga actgttatag aaaaagaatt tgtatcacct tccttaacac caccccagc
cattgctcat cccgcactac ccactattcc agaacgaaag gaagttctgt tggaagcatc
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tgaagaaact ggaaagaggg tttcaaagtt t
                                                                        451
<210> 1039
<211> 533
<212> DNA
<213> Homo sapien
<400> 1039
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                                                                        120
aagcctcttt ttacctgctt gacaggtaat ttctgtaatt ggttgtgatt gaatttgata
                                                                        180
gggtagagaa ttaaatgagg gaagctgtgt atacttccta gtaagagcta ttatatgact
                                                                        240
                                                                        300
qattacatta acatcatatg gaaaaaaatt gtcaaaagta ctccgggaaa gcccttaaat
                                                                        360
agttggtaaa gtacagaaca catgattgtc aatatatgta aatacaggat gagctaggac
agaggggccc ttctttcaca ccacttaaat tagttcccac tttaaccttg tttgagattg
                                                                        420
acttctqqaq agttaaatqc agatagactt aactctccta agtcaggtga gactgagagc
                                                                        480
                                                                        533
tgactgctac aataattacg gagcccaaat gcagtaaaac agcctgtttt tca
<210> 1040
<211> 317
<212> DNA
<213> Homo sapien
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<220>

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<221> misc feature
 <222> (1)...(317)
 <223> n = A, T, C or G
 <400> 1040
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 ggccttcctt ttgaggagct ggagggtgg ggagctagag gccacctatg ccagtgctca
                                                                        120
 aggttactgg gagtgtgggc tgcccttgnt gcctgcaccc ttccctcttc cctctcctc
                                                                        180
 tctctgggac cactgggtac aagagatggg atgctccgac agcgtctnca attatgaaac
                                                                        240
 taatcttaac ccctgtgctg tcagataccc tgtttctgga gtcacatcag tgaggaggga
                                                                        300
. tgtgggtaag aggagca
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<210> 1041
<211> 407
 <212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(407)
<223> n = A, T, C or G
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                                                                         60
catggacatg aactetetta acatgtantt etttgggtge attttgtetg aaccacaatt
                                                                        120
gtgaaggcag ctcagcttag tgcacaaatt ttaactgttg tatataaagc aaataagtca
                                                                        180
gcanatgggt gaagaggtcc agaatgatat gcaaaaacta ctttttagag aaacananca
                                                                        240
actttgtagc aacaaattaa atatagtatt agattgttac ttacgtagat tttattttta
                                                                       300
ctatgcctta ccaagtacat ccttaaacaa agtagtatgt acatgaaatt gcacttaacc
                                                                       360
aaaactattg tgtaaaacaa atttttaatt cctcagggtt ttaattt
                                                                       407
<210> 1042
<211> 519
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(519)
<223> n = A, T, C or G
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acatcatcaa gtatgagaag cctgggtctc ctcccagaga agtggtccct cggccccgcc
                                                                       120
ctggtgtcac agaggctact attactggcc tggaaccggg aaccgaatat acaatttatg
                                                                       180
tcattgccct gaagaataat cagaagagcg agcccctgat tggaaggaaa aagacagacg
                                                                       240
agettececa actggtaace ettecacace ceaatettea tggaceagag atettggatg
                                                                       300
tteetteeac agtteaaaag acceetteg teacceacce tgggtatgac actggaaatg
                                                                       360
gtattcagct tcctggcact tctggtcagc aacccagtgt tgggcaacaa atgatctttg
                                                                       420
aggaacatgg ttttaggcgg accacacgg cccacaacgg ncacccccat aaaggcatag
                                                                       480
gccaaagacc atacccgccg aatgtaggac aagaaagct
                                                                       519
<210> 1043
<211> 294
<212> DNA
<213> Homo sapien
<400> 1043
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ttccagtctg tctatctttc tccacacagt agcagctatc atagaactct gtgaaagcag
                                                                        120
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gcagaatctc agggaaccgt aaaatgcacc ggcctagttt ccattccttc tcatgatcca
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aaagaatctt ggtttctcga gcagcttttt ggagcatttc ttcatcaata ttgg
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<211> 384
<212> DNA
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cctccatcca gttgttgaag ggtgcagccc gcttggcata ctccaagtac agctggtcaa
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tggtctccag cagtttctcg gtccgctcca gagcttccct tcgcttctga gttagggccc
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ccagattgtc ccactggtca cagatctttt ggcaacgggc gttgacactg ggtgagtcat
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aatagteeag eteattgage teetgtgega tggeggeaat etgeteeaca eggteetggt
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gggcagccag gtcactctcg aagg
                                                                        384
<210> 1045
<211> 456
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(456)
<223> n = A, T, C or G
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                                                                        120
aaaatccaag tgtcctcctc caccactcac gctggtgatc actgtgctct ctgccagctg
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cgtggagtga cgggaggagg gaatcactgt gtgtgcgaga gtgcttcaga ctcaatttcc
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aaaataattt tcacccctct aagcatgtaa atatacaaag atggatcctt catagaaatt
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aaaaaaatcaa tttgagctca tttcgaatac agaacaagta tggcacagat ggaagtcctg
                                                                        360
ccacgtttcc tttaatgatg ctgactcttg tatcacacag gccagcatga agtttcttac
                                                                        420
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                                                                        456
<210> 1046
<211> 136
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(136)
<223> n = A, T, C or G
<400> 1046
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                                                                        120
tcttacatct ctccat
                                                                        136
<210> 1047
<211> 453
<212> DNA
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<213> Homo sapien
<400> 1047
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                                                                     120
tctccgcatt tatattaaaa attcacacac aaatgaaaat ggaaaaactg ccaatacctg
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                                                                     240
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ggcgtgctag ctggatgtct tttggcataa ttgttacacg tttggcatgg atagcacaca
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                                                                     453
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<210> 1048
<211> 219
<212> DNA
<213> Homo sapien
<220>
<221> misc feature
<222> (1)...(219)
\langle 223 \rangle n = A,T,C or G
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                                                                      60
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aaaaaatgtt tootttataa aagoacatgg oggttgaato ttaaggttaa attttaatat
                                                                     180
qaaaqatcct catqaattaa ataqttqatq caatttttaa cqttaattqa tataaaaaaa
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<210> 1049
<211> 2465
<212> DNA
<213> Homo sapiens
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agatgagtca tgatgagcat aaaaagcatt cacatacaaa tttgagtatt tcaacaggag 1440
```

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Ala	Ala 50	Ala	Gln	Asn	Leu	Asp 55	Ser	Ala	Gln	Ser	Pro 60	Gly	Pro	Ser	Trp
Pro 65	Ala	Ala	Tyr	Gly	Ala 70	Pro	Leu	Arg	Glu	Asp 75	Trp	Asn	Gly	Tyr	Ala 80
Pro	Gly	Gly	Ala	Ala 85	Ala	Ala	Asn	Ala	Val 90	Ala	His	Ala	Leu	Asn 95	Gly
Gly	Ser	Pro	Ala 100	Ala	Ala	Met	Gly	Tyr 105	Ser	Ser	Pro	Ala	Asp 110	Tyr	His
Pro	His	His 115	His	Pro	His	His	His 120	Pro	His	His	Pro	Ala 125	Ala	Ala	Pro
Ser	Cys 130	Ala	Ser	Gly	Leu	Leu 135	Gln	Thr	Leu	Asn	Pro 140	Gly	Pro	Pro	Gly
Pro 145	Ala	Ala	Thr	Ala	Ala 150	Ala	Glu	Gln	Leu	Ser 155	Pro	Gly	Gly	Gln	Arg 160
Arg	Asn	Leu	Cys	Glu 165	Trp	Met	Arg	Lys	Pro 170	Ala	Gln	Gln	Ser	Leu 175	Gly
Ser	Gln	Val	Lys 180	Thr	Arg	Thr	Lys	Asp 185	Lys	Tyr	Arg	Val	Val 190	Tyr	Thr
Asp	His	Gln 195	Arg	Leu	Glu	Leu	Glu 200	Lys	Glu	Phe	His	Tyr 205	Ser	Arg	Tyr
Ile	Thr 210	Ile	Arg	Arg	Lys	Ala 215	Glu	Leu	Ala	Ala	Thr 220	Leu	Gly	Leu	Ser
Glu 225	Arg	Gln	Val	Lys	Ile 230	Trp	Phe	Gln	Asn	Arg 235	Arg	Ala	Lys	Glu	Arg 240
Lys	Ile	Asn	Lys	Lys	Lys	Leu	Gln	Pro	Pro						

250

Gln Pro Pro Pro Pro Pro Gln Pro Gln Pro Gln Pro Gly Pro 260 265 270

306

Leu Arg Ser Val Pro Glu Pro Leu Ser Pro Val Ser Ser Leu Gln Ala 275 280

Ser Val Ser Gly Ser Val Pro Gly Val Leu Gly Pro Thr Gly Gly Val

Leu Asn Pro Thr Val Thr Gln

<210> 1062

<211> 237

<212> PRT

<213> Homo sapiens

<400> 1062

Met Ala Gly Val Ser Ala Cys Ile Lys Tyr Ser Met Phe Thr Phe Asn

Phe Leu Phe Trp Leu Cys Gly Ile Leu Ile Leu Ala Leu Ala Ile Trp

Val Arg Val Ser Asn Asp Ser Gln Ala Ile Phe Gly Ser Glu Asp Val

Gly Ser Ser Ser Tyr Val Ala Val Asp Ile Leu Ile Ala Val Gly Ala

Ile Ile Met Ile Leu Gly Phe Leu Gly Cys Cys Gly Ala Ile Lys Glu

Ser Arg Cys Met Leu Leu Phe Phe Ile Gly Leu Leu Ile Leu

Leu Leu Gln Val Ala Thr Gly Ile Leu Gly Ala Val Phe Lys Ser Lys

Ser Asp Arg Ile Val Asn Glu Thr Leu Tyr Glu Asn Thr Lys Leu Leu 115 120

Ser Ala Thr Gly Glu Ser Glu Lys Gln Phe Gln Glu Ala Ile Ile Val 135

Phe Gln Glu Glu Phe Lys Cys Cys Gly Leu Val Asn Gly Ala Ala Asp 145 150 155 160

Trp Gly Asn Asn Phe Gln His Tyr Pro Glu Leu Cys Ala Cys Leu Asp 165

Lys Gln Arg Pro Cys Gln Ser Tyr Asn Gly Lys Gln Val Tyr Lys Glu 185

Thr Cys Ile Ser Phe Ile Lys Asp Phe Leu Ala Lys Asn Leu Ile Ile 195

Val Ile Gly Ile Ser Phe Gly Leu Ala Val Ile Glu Ile Leu Gly Leu 215

PCT/US00/35596 WO 01/49716

307

Val Phe Ser Met Val Leu Tyr Cys Gln Ile Gly Asn Lys 225 230

<210> 1063

<211> 80

<212> PRT

<213> Homo sapiens

<400> 1063

Met Ala Ala Arg Ala Leu Cys Met Leu Gly Leu Val Leu Ala Leu Leu

Ser Ser Ser Ser Ala Glu Glu Tyr Val GÎy Leu Ser Ala Asn Gln Cys

Ala Val Pro Ala Lys Asp Arg Val Asp Cys Gly Tyr Pro His Val Thr

Pro Lys Glu Cys Asn Asn Arg Gly Cys Cys Phe Asp Ser Arg Ile Pro 50 60

Gly Val Pro Trp Cys Phe Lys Pro Leu Gln Glu Ala Glu Cys Thr Phe 70

<210> 1064

<211> 323

<212> PRT

<213> Homo sapiens

<400> 1064

Met Ala Tyr Val Pro Ala Pro Gly Tyr Gln Pro Thr Tyr Asn Pro Thr 5

Leu Pro Tyr Tyr Gln Pro Ile Pro Gly Gly Leu Asn Val Gly Met Ser

Val Tyr Ile Gln Gly Val Ala Ser Glu His Met Lys Arg Phe Phe Val

Asn Phe Val Val Gly Gln Asp Pro Gly Ser Asp Val Ala Phe His Phe 50

Asn Pro Arg Phe Asp Gly Trp Asp Lys Val Val Phe Asn Thr Leu Gln

Gly Gly Lys Trp Gly Ser Glu Glu Arg Lys Arg Ser Met Pro Phe Lys 85 90

Lys Gly Ala Ala Phe Glu Leu Val Phe Ile Val Leu Ala Glu His Tyr 100 105

Lys Val Val Val Asn Gly Asn Pro Phe Tyr Glu Tyr Gly His Arg Leu 120

Pro Leu Gln Met Val Thr His Leu Gln Val Asp Gly Asp Leu Gln Leu 130 135 140

308

Gln Ser Ile Asn Phe Ile Gly Gly Gln Pro Leu Arg Pro Gln Gly Pro Pro Met Met Pro Pro Tyr Pro Gly Pro Gly His Cys His Gln Gln Leu 170 Asn Ser Leu Pro Thr Met Glu Gly Pro Pro Thr Phe Asn Pro Pro Val Pro Tyr Phe Gly Arg Leu Gln Gly Gly Leu Thr Ala Arg Arg Thr Ile Ile Ile Lys Gly Tyr Val Pro Pro Thr Gly Lys Ser Phe Ala Ile Asn Phe Lys Val Gly Ser Ser Gly Asp Ile Ala Leu His Ile Asn Pro Arg 230 Met Gly Asn Gly Thr Val Val Arg Asn Ser Leu Leu Asn Gly Ser Trp Gly Ser Glu Glu Lys Lys Ile Thr His Asn Pro Phe Gly Pro Gly Gln Phe Phe Asp Leu Ser Ile Arg Cys Gly Leu Asp Arg Phe Lys Val Tyr 280 Ala Asn Gly Gln His Leu Phe Asp Phe Ala His Arg Leu Ser Ala Phe 290 Gln Arg Val Asp Thr Leu Glu Ile Gln Gly Asp Val Thr Leu Ser Tyr 310 315. Val Gln Ile <210> 1065 <211> 957 <212> PRT <213> Homo sapiens

<400> 1065

Arg Asn Arg Pro His Thr Thr Ala Phe Pro Gly Ser Thr Thr Met Pro

Gly Val Ser Gln Glu Ser Thr Ala Ser His Ser Ser Pro Gly Ser Thr 20 25 30

Asp Thr Thr Leu Ser Pro Gly Ser Thr Thr Ala Ser Ser Leu Gly Pro

Glu Ser Thr Thr Phe His Ser Gly Pro Gly Ser Thr Glu Thr Thr Leu 55

Leu Pro Asp Asn Thr Thr Ala Ser Gly Leu Leu Glu Ala Ser Thr Pro 65 70 75

Va	1 Hi	s Se	r Se	r Thi	Gly	/ Se:	r Pr	o Hi	s Th 9	r Th O	r Le	u Se	r Pr	o Al 9	a Gly 5
Se	r Th	r Th	r Ar	g Glr O	ı Gly	g Gli	ı Se	r Th 10	r Th 5	r Ph	e Glı	n Se	r Tr		o Asn
Se	r Ly	s As 11	p Thi	r Thr	Pro	Ala	a Pro	o Pro	o Th	r Th	r Thi	Se.		a Ph	e Val
Glı	u Le	u Se. O	r Thi	r Thr	Ser	His 135	Gly	y Se:	r Pr	o Se:	r Ser 140		r Pr	o Th:	r Thr
His 149	s Pho	e Se:	r Ala	a Ser	Ser 150	Thr	Thi	: Le	ı Gl	y Arc 15	g Ser 5	: Gl	ı Glı	ı Sei	Thr 160
Thi	· Vai	l His	s Ser	Ser 165	Pro	Val	. Ala	Thi	Ala 170	a Thi	Thr	Pro	Sei	2 Pro	Ala
Arg	g Sei	: Thi	Thr 180	Ser	Gly	Leu	Val	. Glu 185	ı Glu	ı Ser	Thr	Thi	Tyı 190		Ser
		195)				200					205	5		Thr
Ser	Gly 210	Arg	g Gly	Glu	Glu	Ser 215	Thr	Thr	Ser	His	Ser 220	Ser	Thr	Thr	His
Thr 225	Ile	: Ser	Ser	Ala	Pro 230	Ser	Thr	Thr	Ser	Ala 235	Leu	Val	Glu	Glu	Pro 240
Thr	Ser	Tyr	His	Ser 245	Ser	Pro	Gly	Ser	Thr 250		Thr	Thr	His	Phe 255	Pro
			260	Thr				265					270		
		273		Ala			280					285			
	200			Leu		295					300				
000					310			•		315					320
				Thr 325					330					335	
			240	Ala				345					350		
		333		Ser :			360					365			
Asp	Ser 370	Thr	Thr	Thr 1	Pro G	31y : 375	Leu	Ser	Arg	His	Ser 380	Thr	Thr	Ser	His

	Ser 385	Ser	Pro	Gly	Ser	Thr 390	Asp	Thr	Thr	Leu	Leu 395	Pro	Ala	Ser	Thr	Thr 400
	Thr	Ser	Gly	Pro	Ser 405	Gln	Glu	Ser	Thr	Thr 410	Ser	His	Ser	Ser	Pro 415	Gly
	Ser	Thr	Asp	Thr 420	Ala	Leu	Ser	Pro	Gly 425	Ser	Thr	Thr	Ala	Leu 430	Ser	Phe
	Gly	Gln	Glu 435	Ser	Thr	Thr	Phe	His 440	Ser	Ser	Pro	Gly	Ser 445	Thr	His	Thr
	Thr	Leu 450	Phe	Pro	Asp	Ser	Thr 455	Thr	Ser	Ser	Gly	Ile 460	Val	Glu	Ala	Ser
	Thr 465	Arg	Val	His	Ser	Ser 470	Thr	Gly	Ser	Pro	Arg 475	Thr	Thr	Leu	Ser	Pro 480
	Ala	Ser	Ser	Thr	Ser 485	Pro	Gly	Leu	Gln	Gly 490	Glu	Ser	Thr	Ala	Phe 495	Gln
	Thr	His	Pro	Ala 500	Ser	Thr	His	Thr	Thr 505	Pro	Ser	Thr	Pro	Ser 510	Thr	Ala
	Thr	Ala	Pro 515	Val	Glu	Glu	Ser	Thr 520	Thr	Tyr	His	Arg	Ser 525	Pro	Ser	Ser
	Thr	Pro 530	Thr	Thr	His	Phe	Pro 535	Ala	Ser	Ser	Thr	Thr 540	Ser	Gly	His	Ser
	Glu 545	Lys	Ser	Thr	Ile	Phe 550	His	Ser	Ser	Pro	Asp 555	Ala	Ser	Gly	Thr	Thr 560
	Pro	Ser	Ser	Ala	His 565	Ser	Thr	Thr	Ser	Gly 570	Arg	Gly	Glu	Ser	Thr 575	Thr
	Ser	Arg	Ile	Ser 580	Pro	Gly	Ser	Thr	Glu 585	Ile	Thr	Thr	Leu	Pro 590	Gly	Ser
	Thr	Thr	Thr 595	Pro	Gly	Leu	Ser	Glu 600	Ala	Ser	Thr	Thr	Phe 605	Tyr	Ser	Ser
	Pro	Arg 610	Ser	Pro	Thr	Thr	Thr 615	Leu	Ser	Pro	Ala	Ser 620	Met	Thr	Ser	Leu
	Gly 625	Val	Gly	Glu	Glu	Ser 630	Thr	Thr	Ser	Arg	Ser 635	Gln	Pro	Gly	Ser	Thr 640
	His	Ser	Thr	Val	Ser 645	Pro	Ala	Ser	Thr	Thr 650	Thr	Pro	Gly	Leu	Ser 655	Glu
	Glu	Ser	Thr	Thr 660	Val	Tyr	Ser	Ser	Ser 665	Pro	Gly	Ser	Thr	Glu 670	Thr	Thr
•	Val	Phe	Pro 675	Arg	Ser	Thr	Thr	Thr 680	Ser	Val	Arg	Gly	Glu 685	Glu	Pro	Thr
	Thr	Phe	His	Ser	Arg	Pro	Ala	Ser	Thr	His	Thŗ	Thr	Leu	Phe	Thr	Glu

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690 695 700 Asp Ser Thr Thr Ser Gly Leu Thr Glu Glu Ser Thr Ala Phe Pro Gly 710 Ser Pro Ala Ser Thr Gln Thr Gly Leu Pro Ala Thr Leu Thr Thr Ala 730 Asp Leu Gly Glu Glu Ser Thr Thr Phe Pro Ser Ser Ser Gly Ser Thr 740 745 Gly Thr Thr Leu Ser Pro Ala Arg Ser Thr Thr Ser Gly Leu Val Gly 760 Glu Ser Thr Pro Ser Arg Leu Ser Pro Ser Ser Thr Glu Thr Thr 775 Leu Pro Gly Ser Pro Thr Thr Pro Ser Leu Ser Glu Lys Ser Thr Thr 790 Phe Tyr Thr Ser Pro Arg Ser Pro Asp Ala Thr Leu Ser Pro Ala Thr 810 Thr Thr Ser Ser Gly Val Ser Glu Glu Ser Ser Thr Ser His Ser Gln 820 Pro Gly Ser Thr His Thr Thr Ala Phe Pro Asp Ser Thr Thr Thr Ser 840 Gly Leu Ser Gln Glu Pro Lys Thr Ser His Ser Ser Gln Gly Ser Thr 855 Glu Ala Thr Leu Ser Pro Gly Ser Thr Thr Ala Ser Ser Leu Gly Gln 865 Gln Ser Thr Thr Phe His Ser Ser Pro Gly Asp Thr Glu Thr Thr Leu 885 890 Leu Pro Asp Asp Thr Ile Thr Ser Gly Leu Val Glu Ala Ser Thr Pro 900 905 Thr His Ser Ser Thr Gly Ser Leu His Thr Thr Leu Thr Pro Ala Ser Ser Thr Ser Ala Gly Leu Gln Glu Glu Ser Thr Thr Phe Gln Ser Trp 935 Pro Ser Ser Ser Asp Thr Thr Pro Ser Pro Pro Gly Pro 945 950 <210> 1066 <211> 914 <212> PRT <213> Homo sapiens

Met Gly Pro Phe Lys Ser Ser Val Phe Ile Leu Ile Leu His Leu Leu

<400> 1066

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Glu	Gly	Ala	Leu 20	Ser	Asn	Ser	Leu	Ile 25	Gln	Leu	Asn	Asn	Asn 30	Gly	Туз
Glu	Gly	Ile 35	Val	Val	Ala	Ile	Asp 40	Pro	Asn	Val	Pro	Glu 45	Asp	Glu	Thi
Leu	Ile 50	Gln	Gln	Ile	Lys	Asp 55	Met	Val	Thr	Gln	Ala 60	Ser	Leu	Tyr	Let
Phe 65	Glu	Ala	Thr	Gly	Lys 70	Arg	Phe	Tyr	Phe	Lys 75	Asn	Val	Ala	Ile	Let 80
Ile	Pro	Glu	Thr	Trp 85	Lys	Thr	Lys	Ala	Asp 90	Tyr	Val	Arg	Pro	Lys 95	Let
Glu	Thr	Tyr	Lys 100	Asn	Ala	Asp	Val	Leu 105	Val	Ala	Glu	Ser	Thr 110	Pro	Pro
Gly	Asn	Asp 115	Glu	Pro	Tyr	Thr	Glu 120	Gln	Met	Gly	Asn-	Cys 125	Gly	Glu	Lys
Gly	Glu 130	Arg	Ile	His	Leu	Thr 135	Pro	Asp	Phe	Ile	Ala 140	Gly	Lys	Lys	Let
Ala 145	Glu	Tyr	Gly	Pro	Gln 150	Gly	Lys	Ala	Phe	Val 155	His	Glu	Trp	Ala	His 160
Leu	Arg	Trp	Gly	Val 165	Phe	Asp	Glu	Tyr	Asn 170	Asn	Asp	Glu	Lys	Phe 175	Туг
Leu	Ser	Asn	Gly 180	Arg	Ile	Gln	Ala	Val 185	Arg	Cys	Ser	Ala	Gly 190	Ile	Thi
Gly	Thr	Asn 195	Val	Val	Lys	Lys	Cys 200	Gln	Gly	Gly	Ser	Cys 205	Tyr	Thr	Lys
Arg	Cys 210	Thr	Phe	Asn	Lys	Val 215	Thr	Gly	Leu	Tyr	Glu 220	Lys	Gly	Cys	Glu
Phe 225	Val	Leu	Gln	Ser	Arg 230	Gln	Thr	Glu	Lys	Ala 235	Ser	Ile	Met	Phe	Ala 240
Gln	His	Val	Asp	Ser 245	Ile	Val	Glu	Phe	Cys 250	Thr	Glu	Gln	Asn	His 255	Asn
Lys	Glu	Ala	Pro 260	Asn	Lys	Gln	Asn	Gln 265	Lys	Cys	Asn	Leu	Arg 270	Ser	Thr
Trp	Glu	Val 275	Ile	Arg	Asp	Ser	Glu 280	Asp	Phe	Lys	Lys	Thr 285	Thr	Pro	Met
Thr	Thr 290	Gln	Pro	Pro	Asn	Pro 295	Thr	Phe	Ser	Leu	Leu 300	Gln	Ile	Gly	Gln
Arg 305	Ile	Val	Cys	Leu	Val 310	Leu	Asp	Lys	Ser	Gly 315	Ser	Met	Ala	Thr	Gly 320

Asn	Arg	Leu	Asn	Arg 325	Leu	Asn	Gln	Ala	Gly 330	Gln	Leu	Phe	Leu	Leu 335	Gln
Thr	Val	Glu	Leu 340	Gly	Ser	Trp	Val	Gly 345	Met	Val	Thr	Phe	Asp 350	Ser	Ala
Ala	His	Val 355	Gln	Ser	Glu	Leu	Ile 360	Gln	Ile	Asn	Ser	Gly 365	Ser	Asp	Arg
Asp	Thr 370	Leu	Ala	Lys	Arg	Leu 375	Pro	Ala	Ala	Ala	Ser 380	Gly	Gly	Thr	Ser
Ile 385	Cys	Ser	Gly	Leu	Arg 390	Ser	Ala	Phe	Thr	Val 395	Ile	Arg	Lys	Lys	Tyr 400
Pro	Thr	Asp	Gly	Ser 405	Glu	Ile	Val	Leu	Leu 410	Thr	Asp	Gly	Glu	Asp 415	Asn
Thr	Ile	Ser	Gly 420	Суз	Phe	Asn	Glu	Val 425	Lys	Gln	Ser	Gly	Ala 430	Ile	Ile
His	Thr	Val 435	Ala	Leu	Gly	Pro	Ser 440	Ala	Ala	Gln	Glu	Leu 445	Glu	Glu	Leu
Ser	Lys 450	Met	Thr	Gly	Gly	Leu 455	Gln	Thr	Tyr	Ala	Ser 460	Asp	Gln	Val	Gln
Asn 465	Asn	Gly	Leu	Ile	Asp 470	Ala	Phe	Gly	Ala	Leu 475	Ser	Ser	Gly	Asn	Gly 480
Ala	Val	Ser	Gln	Arg 485	Ser	Ile	Gln	Leu	Glu 490	Ser	Lys	Gly	Leu	Thr 495	Leu
Gln	Asn	Ser	Gln 500	Trp	Met	Asn	Gly	Thr 505	Val	Ile	Val	Asp	Ser 510	Thr	Val
Gly	Lys	Asp 515	Thr	Leu	Phe	Leu	Ile 520	Thr	Trp	Thr	Thr	Gln 525	Pro	Pro	Gln
Ile	Leu 530	Leu	Trp	Asp	Pro	Ser 535	Gly	Gln	Lys	Gln	Gly 540	Gly	Phe	Val	Val
Asp 545	Lys	Asn	Thr	Lys	Met 550	Ala	Tyr	Leu	Gln	Ile 555	Pro	Gly	Ile	Ala	Lys 560
Val	Gly	Thr	Trp	Lys 565	Tyr	Ser	Leu	Gln	Ala 570	Ser	Ser	Gln	Thr	Leu 575	Thr
Leu	Thr	Val	Thr 580	Ser	Arg	Ala	Ser	Asn 585	Ala	Thr	Leu	Pro	Pro 590	Ile	Thr
Val	Thr	Ser 595	Lys	Thr	Asn	Lys	Asp 600	Thr	Ser	Lys	Phe	Pro 605	Ser	Pro	Leu
Val	Val 610	Tyr	Ala	Asn	Ile	Arg 615	Gln	Gly	Ala	Ser	Pro 620	Ile	Leu	Arg	Ala

314

Ser Val Thr Ala Leu Ile Glu Ser Val Asn Gly Lys Thr Val Thr Leu 625 630 635 640

Glu Leu Leu Asp Asn Gly Ala Gly Ala Asp Ala Thr Lys Asp Asp Gly
645 650 655

Val Tyr Ser Arg Tyr Phe Thr Thr Tyr Asp Thr Asn Gly Arg Tyr Ser 660 665 670

Val Lys Val Arg Ala Leu Gly Gly Val Asn Ala Ala Arg Arg Val 675 680 685

Ile Pro Gln Gln Ser Gly Ala Leu Tyr Ile Pro Gly Trp Ile Glu Asn 690 695 700

Asp Glu Ile Gln Trp Asn Pro Pro Arg Pro Glu Ile Asn Lys Asp Asp 705 710 715 720

Val Gln His Lys Gln Val Cys Phe Ser Arg Thr Ser Ser Gly Gly Ser
725 730 735

Phe Val Ala Ser Asp Val Pro Asn Ala Pro Ile Pro Asp Leu Phe Pro 740 745 750

Pro Gly Gln Ile Thr Asp Leu Lys Ala Glu Ile His Gly Gly Ser Leu
755 760 765

Ile Asn Leu Thr Trp Thr Ala Pro Gly Asp Asp Tyr Asp His Gly Thr 770 780

Ala His Lys Tyr Ile Ile Arg Ile Ser Thr Ser Ile Leu Asp Leu Arg
785 790 795 800

Asp Lys Phe Asn Glu Ser Leu Gln Val Asn Thr Thr Ala Leu Ile Pro 805 810 815

Lys Glu Ala Asn Ser Glu Glu Val Phe Leu Phe Lys Pro Glu Asn Ile 820 825 830

Thr Phe Glu Asn Gly Thr Asp Leu Phe Ile Ala Ile Gln Ala Val Asp 835 840 845

Lys Val Asp Leu Lys Ser Glu Ile Ser Asn Ile Ala Arg Val Ser Leu 850 855 860

Phe Ile Pro Pro Gln Thr Pro Pro Glu Thr Pro Ser Pro Asp Glu Thr 865 870 875 880

Ser Ala Pro Cys Pro Asn Ile His Ile Asn Ser Thr Ile Pro Gly Ile 885 890 895

His Ile Leu Lys Ile Met Trp Lys Trp Ile Gly Glu Leu Gln Leu Ser 900 905 910

Ile Ala

315

<210> 1067

<211> 585

<212> PRT

<213> Homo sapiens

<400> 1067

Thr Leu Ser Pro Ala Ser Met Arg Ser Ser Ser Ile Ser Gly Glu Pro
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Thr Ser Leu Tyr Ser Gln Ala Glu Ser Thr His Thr Thr Ala Phe Pro 20 25 30

Ala Ser Thr Thr Ser Gly Leu Ser Gln Glu Ser Thr Thr Phe His
35 40 45

Ser Lys Pro Gly Ser Thr Glu Thr Thr Leu Ser Pro Gly Ser Ile Thr 50 55 60

Thr Ser Ser Phe Ala Gln Glu Phe Thr Thr Pro His Ser Gln Pro Gly 65 70 75 80

Ser Ala Leu Ser Thr Val Ser Pro Ala Ser Thr Thr Val Pro Gly Leu 85 90 95

Ser Glu Glu Ser Thr Thr Phe Tyr Ser Ser Pro Gly Ser Thr Glu Thr 100 105 110

Thr Ala Phe Ser His Ser Asn Thr Met Ser Ile His Ser Gln Gln Ser 115 120 125

Thr Pro Phe Pro Asp Ser Pro Gly Phe Thr His Thr Val Leu Pro Ala 130 135 140

Thr Leu Thr Thr Thr Asp Ile Gly Gln Glu Ser Thr Ala Phe His Ser 145 150 155 160

Ser Ser Asp Ala Thr Gly Thr Thr Pro Leu Pro Ala Arg Ser Thr Ala 165 170 175

Ser Asp Leu Val Gly Glu Pro Thr Thr Phe Tyr Ile Ser Pro Ser Pro 180 185 190

Thr Tyr Thr Thr Leu Phe Pro Ala Ser Ser Ser Thr Ser Gly Leu Thr 195 200 205

Glu Glu Ser Thr Thr Phe His Thr Ser Pro Ser Phe Thr Ser Thr Ile 210 215 220

Val Ser Thr Glu Ser Leu Glu Thr Leu Ala Pro Gly Leu Cys Gln Glu 225 230 235 240

Gly Gln Ile Trp Asn Gly Lys Gln Cys Val Cys Pro Gln Gly Tyr Val 245 250 255

Gly Tyr Gln Cys Leu Ser Pro Leu Glu Ser Phe Pro Val Glu Thr Pro 260 265 270

Glu Lys Leu Asn Ala Thr Leu Gly Met Thr Val Lys Val Thr Tyr Arg

		275					280					285			
Asn	Phe 290	Thr	Glu	Lys	Met	Asn 295	Asp	Ala	Ser	Ser	Gln 300	Glu	Tyr	Gln	Asr
Phe 305	Ser	Thr	Leu	Phe	Lys 310	Asn	Arg	Met	Asp	Val 315	Val	Leu	Lys	Gly	Asp 320
Asn	Leu	Pro	Gln	Tyr 325	Arg	Gly	Val	Asn	Ile 330	Arg	Arg	Leu	Leu	Asn 335	Gly
Ser	Ile	Val	Val 340	Lys	Asn	Asp	Val	Ile 345	Leu	Glu	Ala	Asp	Tyr 350	Thr	Leu
Glu	Tyr	Glu 355	Glu	Leu	Phe	Glu	Asn 360	Leu	Ala	Glu	Ile	Val 365	Lys	Ala	Lys
Ile	Met 370	Asn	Glu	Thr	Arg	Thr 375	Thr	Leu	Leu	Asp	Pro 380	Asp	Ser	Суз	Arç
Lys 385	Ala	Ile	Leu	Cys	Tyr 390	Ser	Glu	Glu	Asp	Thr 395	Phe	Val	Asp	Ser	Ser 400
Val	Thr	Pro	Gly	Phe 405	Asp	Phe	Gln	Glu	Gln 410	Cys	Thr	Gln	Lys	Ala 415	Ala
Glu	Gly	Tyr	Thr 420	Gln	Phe	Tyr	Tyr	Val 425	Asp	Val	Leu	Asp	Gly 430	Lys	Leu
Ala	Cys	Val 435	Asn	Lys	Суз	Thr	Lys 440	Gly	Thr	Lys	Ser	Gln 445	Met	Asn	Cys
Asn	Leu 450	Gly	Thr	Cys	Gln	Leu 455	Gln	Arg	Ser	Gly	Pro 460	Arg	Cys	Leu	Cys
Pro 465	Asn	Thr	Asn	Thr	His 470	Trp	Tyr	Trp	Gly	Glu 475	Thr	Суз	Glu	Phe	Asn 480
Ile	Ala	Lys	Ser	Leu 485	Val	Tyr	Gly	Ile	Val 490	Gly	Ala	Val	Met	Ala 495	Val
Leu	Leu	Leu	Ala 500	Leu	Ile	Ile	Leu	Ile 505	Ile	Leu	Phe	Ser	Leu 510	Ser	Gln
Arg	Lys	Arg 515	His	Arg	Glu	Gln	Tyr 520	Asp	Val	Pro	Gln	Glu 525	Trp	Arg	Lys
Glu	Gly 530	Thr	Pro	Gly	Ile	Phe 535	Gln	Lys	Thr	Ala	Ile 540	Trp	Glu	Asp	Gln
Asn 545	Leu	Arg	Glu	Ser	Arg 550	Phe	Gly	Leu	Glu	Asn 555	Ala	Tyr	Asn	Asn	Phe 560
Arg	Pro	Thr	Leu	Glu 565	Thr	Val	Asp	Ser	Gly 570	Thr	Glu	Leu	His	Ile 575	Gln
Arg	Pro	Glu	Met 580	Val	Ala	Ser	Thr	Val 585							

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Met Gly Leu Pro Leu Ala Arg Leu Ala Ala Val Cys Leu Ala Leu Ser 5 10 15

Leu Ala Gly Gly Ser Glu Leu Gln Thr Glu Gly Arg Thr Arg Tyr His 20 25 30

Gly Arg Asn Val Cys Ser Thr Trp Gly Asn Phe His Tyr Lys Thr Phe 35 40 45

Asp Gly Asp Val Phe Arg Phe Pro Gly Leu Cys Asp Tyr Asn Phe Ala 50 55 60

Ser Asp Cys Arg Gly Ser Tyr Lys Glu Phe Ala Val His Leu Lys Arg 65 70 75 80

Gly Pro Gly Gln Ala Glu Ala Pro Ala Gly Val Glu Ser Ile Leu Leu 85 90 95

Thr Ile Lys Asp Asp Thr Ile Tyr Leu Thr Arg His Leu Ala Val Leu 100 105 110

Asn Gly Ala Val Val Ser Thr Pro His Tyr Ser Pro Gly Leu Leu Ile 115 120 125

Glu Lys Ser Asp Ala Tyr Thr Lys Val Tyr Ser Arg Ala Gly Leu Thr 130 135 140

Leu Met Trp Asn Arg Glu Asp Ala Leu Met Leu Glu Leu Asp Thr Lys 145 150 155 160

Phe Arg Asn His Thr Cys Gly Leu Cys Gly Asp Tyr Asn Gly Leu Gln 165 170 175

Ser Tyr Ser Glu Phe Leu Ser Asp Gly Val Leu Phe Ser Pro Leu Glu 180 185 190

Phe Gly Asn Met Gln Lys Ile Asn Gln Pro Asp Val Val Cys Glu Asp 195 200 . 205

Pro Glu Glu Glu Val Ala Pro Ala Ser Cys Ser Glu His Arg Ala Glu 210 215 220

Cys Glu Arg Leu Leu Thr Ala Glu Ala Phe Ala Asp Cys Gln Asp Leu 225 230 235 240

Val Pro Leu Glu Pro Tyr Leu Arg Ala Cys Gln Gln Asp Arg Cys Arg 245 250 255

Cys Pro Gly Gly Asp Thr Cys Val Cys Ser Thr Val Ala Glu Phe Ser 260 265 270

Arg	Gln	Cys 275	Ser	His	Ala	Gly	Gly 280	Arg	Pro	Gly	Asn	Trp 285	Arg	Thr	Ala
Thr	Leu 290	Cys	Pro	Lys	Thr	Cys 295	Pro	Gly	Asn	Leu	Val 300	Tyr	Leu	Glu	Ser
Gly 305	Ser	Pro	Cys	Met	Asp 310	Thr	Cys	Ser	His	Leu 315	Glu	Val	Ser	Ser	Leu 320
Cys	Glu	Glu	His	Arg 325	Met	Asp	Gly	Cys	Phe 330	Cys	Pro	Glu	Gly	Thr 335	Val
Tyr	Asp	Asp	Ile 340	Gly	Asp	Ser	Gly	Cys 345	Val	Pro	Val	Ser	Gln 350	Cys	His
Cys	Arg	Leu 355	His	Gly	His	Leu	Tyr 360	Thr	Pro	Gly	Gln	Glu 365	Ile	Thr	Asn
Asp	Cys 370	Glu	Gln	Суѕ	Val	Cys 375	Asn	Ala	Gly	Arg	Trp 380	Val	Cys	Lys	Asp
Leu 385	Pro	Cys	Pro	Gly	Thr 390	Суѕ	Ala	Leu	Glu	Gly 395	Gly	Ser	His	Ile	Thr 400
Thr	Phe	Asp	Gly	Lys 405	Thr	Tyr	Thr	Phe	His 410	Gly	Asp	Cys	Tyr	Tyr 415	Val
Leu	Ala	Lys	Gly 420	Asp	His	Asn	Asp	Ser 425	Tyr	Ala	Leu	Leu	Gly 430	Glu	Leu
Ala	Pro	Cys 435	Gly	Ser	Thr	Asp	Lys 440	Gln	Thr	Cys	Leu	Lys 445	Thr	Val	Val
Leu	Leu 450	Ala	Asp	Lys	Lys	Lys 455	Asn	Ala	Val	Val	Phe 460	Lys	Ser	Asp	Gly
Ser 465	Val	Leu	Leu	Asn	Gln 470	Leu	Gln	Val	Asn	Leu 475	Pro	His	Val	Thr	Ala 480
Ser	Phe	Ser	Val	Phe 485	Arg	Pro	Ser	Ser	Tyr 490	His	Ile	Met	Val	Ser 495	Met
Ala	Ile	Gly	Val 500	Arg	Leu	Gln	Val.	Gln 505	Leu	Ala	Pro	Val	Met 510	Gln	Leu
Phe	Val	Thr 515	Leu	Asp	Gln	Ala	Ser 520	Gln	Gly	Gln	Val	Gln 525	Gly	Leu	Cys
Gly	Asn 530	Phe	Asn	Gly	Leu	Glu 535	Gly	Asp	Asp	Phe	Lys 540	Thr	Ala	Ser	Gly
Leu 545	Val	Glu	Ala	Thr	Gly 550	Ala	Gly	Phe	Ala	Asn 555	Thr	Trp	Lys	Ala	Gln 560
Ser	Thr	Cys	His	Asp 565	Lys	Leu	Asp	Trp	Leu 570	Asp	Asp	Pro	Cys	Ser 575	Leu

- Asn Ile Glu Ser Ala Asn Tyr Ala Glu His Trp Cys Ser Leu Leu Lys 580 585 590
- Lys Thr Glu Thr Pro Phe Gly Arg Cys His Ser Ala Val Asp Pro Ala 595 600 605
- Glu Tyr Tyr Lys Arg Cys Lys Tyr Asp Thr Cys Asn Cys Gln Asn Asn 610 615 620
- Glu Asp Cys Leu Cys Ala Ala Leu Ser Ser Tyr Ala Arg Ala Cys Thr 625 630 635 640
- Ala Lys Gly Val Met Leu Trp Gly Trp Arg Glu His Val Cys Asn Lys 645 650 655
- Asp Val Gly Ser Cys Pro Asn Ser Gln Val Phe Leu Tyr Asn Leu Thr 660 665 670
- Thr Cys Gln Gln Thr Cys Arg Ser Leu Ser Glu Ala Asp Ser His Cys 675 680 685
- Leu Glu Gly Phe Ala Pro Val Asp Gly Cys Gly Cys Pro Asp His Thr 690 695 700
- Phe Leu Asp Glu Lys Gly Arg Cys Val Pro Leu Ala Lys Cys Ser Cys 705 710 715 720
- Tyr His Arg Gly Leu Tyr Leu Glu Ala Gly Asp Val Val Arg Gln
 725 730 735
- Glu Glu Arg Cys Val Cys Arg Asp Gly Arg Leu His Cys Arg Gln Ile 740 745 750
- Arg Leu Ile Gly Gln Ser Cys Thr Ala Pro Lys Ile His Met Asp Cys 755 760 765
- Ser Asn Leu Thr Ala Leu Ala Thr Ser Lys Pro Arg. Ala Leu Ser Cys 770 780
- Gln Thr Leu Ala Ala Gly Tyr Tyr His Thr Glu Cys Val Ser Gly Cys 785 790 795 800
- Val Cys Pro Asp Gly Leu Met Asp Asp Gly Arg Gly Cys Val Val 805 810 815
- Glu Lys Glu Cys Pro Cys Val His Asn Asn Asp Leu Tyr Ser Ser Gly 820 825 830
- Ala Lys Ile Lys Val Asp Cys Asn Thr Cys Thr Cys Lys Arg Gly Arg 835 840 845
- Trp Val Cys Thr Gln Ala Val Cys His Gly Thr Cys Ser Ile Tyr Gly 850 855 860
- Ser Gly His Tyr Ile Thr Phe Asp Gly Lys Tyr Tyr Asp Phe Asp Gly 865 870 1 875 880
- His Cys Ser Tyr Val Ala Val Gln Asp Tyr Cys Gly Gln Asn Ser Ser

				885					890					895	
Leu	Gly	Ser	Phe 900	Ser	Ile	Ile	Thr	Glu 905	Asn	Val	Pro	Суѕ	Gly 910	Thr	Thr
Gly	Val	Thr 915	Cys	Ser	Lys	Ala	Ile 920	Lys	Ile	Phe	Met	Gly 925	Arg	Thr	Glu
Leu	Lys 930	Leu	Glu	Asp	Lys	His 935	Arg	Val	Val	Ile	Gln 940	Arg	Asp	Glu	Gly
His 945	His	Val	Ala	Tyr	Thr 950	Thr	Arg	Glu	Val	Gly 955	Gln	Tyr	Leu	Val	Val 960
Glu	Ser	Ser	Thr	Gly 965	Ile	Ile	Val	Ile	Trp 970	Asp	Lys	Arg	Thr	Thr 975	Val
Phe	Ile	Lys	Leu 980	Ala	Pro	Ser	Tyr	Lys 985	Gly	Thr	Val	Cys	Gly 990	Leụ	Cys
Gly	Asn	Phe 995	Asp	His	Arg	Ser	Asn 1000		Asp	Phe	Thr	Thr 1005	-	Asp	His
Met	Val 1010		Ser	Ser	Glu	Leu 1015		Phe	Gly	Asn	Ser 1020		Lys	Glu	Ala
Pro 1025		Cys	Pro	Asp	Val 1030		Thr	Asn	Pro	Glu 1035		Cys	Ser	Leu	Asn 1040
Pro	His	Arg	Arg	Ser 1045		Ala	Glu	Lys	Gln 1050		Ser	Ile	Leu	Lys 1055	
		Pho	Ser		Cys	His	Ser	Lys 1065		Asp	Pro	Lys	Pro 1070	Phe	Tyr
Ser	Val	THE	1060)				1007	,				1070		
			Val		Asp	Ser	Cys 1080	Ser		Asp	Thr	Gly 1085	Gly	Asp	Cys
Glu	Ala	Cys 1075 Phe	Val	His			1080 Ala	Ser	Cys			1085 Glu	Gly	Asp Thr	
Glu Glu	Ala Cys 1090 Gly	Cys 1075 Phe	Val	His Ser	Ala	Val 1095 Trp	1080 Ala	Ser Ser	Cys Tyr	Ala	Gln 1100 Leu	1085 Glu	Gly Cys		Ļys
Glu Glu Glu 1105	Ala Cys 1090 Gly	Cys 1075 Phe)	Val Cys Cys	His Ser Val	Ala Phe 1110 Pro	Val 1095 Trp	Ala Arg	Ser Ser Thr	Cys Tyr Pro	Ala Asp 1115 Glu	Gln 1100 Leu	Glu Cys	Gly Cys Pro	Thr	Lys Phe 1120 Pro
Glu Glu Glu 1105 Cys	Cys 1090 Gly Asp	Cys 1075 Phe Ala	Val Cys Cys	His Ser Val Asn 1125	Ala Phe 1110 Pro	Val 1095 Trp Pro	Ala Arg His	Ser Ser Thr	Cys Tyr Pro Cys 1130	Ala Asp 1115 Glu	Gln 1100 Leu Trp	Glu Cys His	Gly Cys Pro	Thr Ile Glu 1135	Lys Phe 1120 Pro
Glu Glu 1105 Cys	Cys 1090 Gly Asp	Cys 1075 Phe Ala Tyr	Val Cys Cys Tyr Arg 1140 Ser	His Ser Val Asn 1125 Ser	Ala Phe 1110 Pro	Val 1095 Trp Pro	Ala Arg His	Ser Ser Thr Glu Cys 1145	Cys Tyr Pro Cys 1130	Ala Asp 1115 Glu Thr	Gln 1100 Leu Trp	Glu Cys His	Gly Cys Pro Tyr Gly 1150	Thr Ile Glu 1135	Lys Phe 1120 Pro
Glu Glu 1105 Cys Cys	Cys 1090 Gly Asp Gly	Cys 1075 Phe Ala Tyr Asn Ile 1155	Val Cys Cys Tyr Arg 1140 Ser	His Ser Val Asn 1125 Ser	Phe 1110 Pro Phe	Val 1095 Trp Pro Glu	Ala Arg His Thr Leu 1160	Ser Ser Thr Glu Cys 1145	Cys Tyr Pro Cys 1130 Arg	Ala Asp 1115 Glu Thr	Gln 1100 Leu Trp Ile	Glu Cys His Asn Pro 1165 Cys	Gly Cys Pro Tyr Gly 1150	Thr Ile Glu 1135 Ile	Lys Phe 1120 Pro His

- Ser Val Pro Thr Glu Glu Thr Cys Lys Ser Cys Val Cys Thr Asn Ser 1205 1210 1215
- Ser Gln Val Cys Arg Pro Glu Glu Gly Lys Ile Leu Asn Gln Thr 1220 1225 1230
- Gln Asp Gly Ala Phe Cys Tyr Trp Glu Ile Cys Gly Pro Asn Gly Thr 1235 1240 1245
- Val Glu Lys His Phe Asn Ile Cys Ser Ile Thr Thr Arg Pro Ser Thr 1250 1255 1260
- Leu Thr Thr Phe Thr Thr Ile Thr Leu Pro Thr Thr Pro Thr Ser Phe 1265 1270 1275 1280
- Thr Thr Thr Thr Thr Thr Thr Pro Thr Ser Ser Thr Val Leu Ser
 1285 1290 1295
- Thr Thr Pro Lys Leu Cys Cys Leu Trp Ser Asp Trp Ile Asn Glu Asp 1300 1305 1310
- His Pro Ser Ser Gly Ser Asp Asp Gly Asp Arg Glu Pro Phe Asp Gly 1315 1320 1325
- Val Cys Gly Ala Pro Glu Asp Ile Glu Cys Arg Ser Val Lys Asp Pro 1330 1335 1340
- His Leu Ser Leu Glu Gln His Gly Gln Lys Val Gln Cys Asp Val Ser 1345 1350 1355 1360
- Val Gly Phe Ile Cys Lys Asn Glu Asp Gln Phe Gly Asn Gly Pro Phe 1365 1370 1375
- Gly Leu Cys Tyr Asp Tyr Lys Ile Arg Val Asn Cys Cys Trp Pro Met 1380 1385 1390
- Asp Lys Cys Ile Thr Thr Pro Ser Pro Pro Thr Thr Thr Pro Ser Pro 1395 1400 1405
- Pro Pro Thr Thr Thr Thr Leu Pro Pro Thr Thr Pro Ser Pro 1410 1415 1420
- Pro Thr Thr Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro 1425 1430 1435 1440
- Pro Ile Thr Thr Thr Thr Pro Leu Pro Thr Thr Pro Ser Pro 1445 1450 1455
- Pro Ile Ser Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro 1460 1465 1470
- Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr 1475 1480 1485
- Thr Thr Thr Thr Pro Pro Pro Thr Thr Pro Ser Pro Pro Met 1490 1495 1500

Thr Thr Pro Ile Thr Pro Pro Ala Ser Thr Thr Thr Leu Pro Pro Thr 1505 1510 1515 1520

Thr Thr Pro Ser Pro Pro Thr Thr Thr Thr Thr Pro Pro Pro Thr
1525 1530 1535

Thr Thr Pro Ser Pro Pro Thr Thr Thr Pro Ile Thr Pro Pro Thr Ser 1540 1550

Thr Thr Thr Leu Pro Pro Thr Thr Pro Ser Pro Pro Pro Thr Thr 1555 1560 1565

Thr Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr 1570 1575 1580

Thr Pro Ser Pro Pro Thr Ile Thr Thr Thr Pro Pro Pro Thr Thr 1585 1590 1595 1600

Thr Pro Ser Pro Pro Thr Thr Thr Thr Thr Pro Pro Pro Thr Thr 1605 1610 1615

Thr Pro Ser Pro Pro Thr Thr Pro Ile Thr Pro Pro Thr Ser Thr 1620 1630

Thr Thr Leu Pro Pro Thr Thr Thr Pro Ser Pro Pro Pro Thr Thr Thr 1635 1640 1645

Thr Thr Pro Pro Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Thr 1650 1655 1660

Pro Ser Pro Pro Ile Thr Thr Thr Thr Pro Pro Pro Thr Thr Thr 1665 1670 1675 1680

Pro Ser Ser Pro Ile Thr Thr Pro Ser Pro Pro Thr Thr Met
1685 1690 1695

Thr Thr Pro Ser Pro Thr Thr Thr Pro Ser Ser Pro Ile Thr Thr Thr 1700 1705 1710

Thr Thr Pro Ser Ser Thr Thr Thr Pro Ser Pro Pro Thr Thr Met 1715 1720 1725

Thr Thr Pro Ser Pro Thr Thr Thr Pro Ser Pro Pro Thr Thr Met 1730 1735 1740

Thr Thr Leu Pro Pro Thr Thr Ser Ser Pro Leu Thr Thr Pro 1745 1750 1755 1760

Leu Pro Pro Ser Ile Thr Pro Pro Thr Phe Ser Pro Phe Ser Thr Thr 1765 1770 1775

Thr Pro Thr Thr Pro Cys Val Pro Leu Cys Asn Trp Thr Gly Trp Leu 1780 1785 1790

Asp Ser Gly Lys Pro Asn Phe His Lys Pro Gly Gly Asp Thr Glu Leu 1795 1800 1805

Ile Gly Asp Val Cys Gly Pro Gly Trp Ala Ala Asn Ile Ser Cys Arg

Ala Thr Met Tyr Pro Asp Val Pro Ile Gly Gln Leu Gly Gln Thr Val Val Cys Asp Val Ser Val Gly Leu Ile Cys Lys Asn Glu Asp Gln Lys Pro Gly Gly Val Ile Pro Met Ala Phe Cys Leu Asn Tyr Glu Ile Asn Val Gln Cys Cys Glu Cys Val Thr Gln Pro Thr Thr Met Thr Thr Thr Thr Glu Asn Pro Thr Pro Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr · 2105

Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr

Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln

Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr

Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr

Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro 2435 2440 2445

Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr 2450 2455 2460

Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr 2465 2470 2475 2480

Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr 2485 2490 2495

Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr 2500 2505 2510

Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Wal 2515 2520 2525

Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro 2530 2535 2540

Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr 2545 2550 2560

Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro 2565 2570 2575

Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr 2580 2590

Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr 2595 2600 2605

Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro 2610 2615 2620

Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr 2625 2630 2635 2640

Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr 2645 2650 2655

Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro 2660 2665 2670

Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr 2675 2680 2685

Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr 2690 2695 2700

Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly 2705 2710 2715 2720

Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr 2725 2730 2735

Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile

			2740)				2745	ō				2750)	
Thr	Thr	Thr 275		Thr	Val	Thr	Pro 2760		Pro	Thr	Pro	Thr 2765		Thr	Gln
Thr	Pro 2770		Thr	Thr	Pro	Ile 2775		Thr	Thr	Thr	Thr 2780		Thr	Pro	Thr
Pro 278		Pro	Thr	Gly	Thr 2790	Gln ₍	Thr	Pro	Thr	Thr 2795		Pro	Ile	Thr	Thr 2800
Thr	Thr	Thr	Val	Thr 280		Thr	Pro	Thr	Pro 2810		Gly	Thr	Gln	Thr 2815	
Thr	Thr	Thr	Pro 2820		Thr	Thr	Thr	Thr 2825		Val	Thr	Pro	Thr 2830		Thr
Pro	Thr	Gly 283		Gln	Thr	Pro	Thr 2840		Thr	Pro	Ile	Thr 2845		Thr	Thr
Thr	Val 2850		Pro	Thr	Pro	Thr 2855		Thr	Gly	Thr	Gln 2860		Pro	Thr	Thr
Thr 286		Ile	Thr	Thr	Thr 2870	Thr	Thr	Val	Thr	Pro 2875		Pro	Thr	Pro	Thr 2880
Gly	Thr	Gln	Thr	Pro 2885		Thr	Thr	Pro	Ile 2890		Thr	Thr	Thr	Thr 2895	
Thr	Pro	Thr	Pro 2900		Pro	Thr	Gly	Thr 2905		Thr	Pro	Thr	Thr 2910		Pro
Ile	Thr	Thr 2915		Thr	Thr	Val	Thr 2920		Thr	Pro	Thr	Pro 2925		Gly	Thr
Gln	Thr 2930		Thr	Thr	Thr	Pro 2935		Thr	Thr	Thr	Thr 2940		Val	Thr	Pro
Thr 2945		Thr	Pro	Thr	Gly 2950	Thr)	Gln	Thr	Pro	Thr 2955		Thr	Pro	Ile	Thr 2960
Thr	Thr	Thr	Thr	Val 2965		Pro	Thr	Pro	Thr 2970		Thr	Gly	Thr	Gln 2975	
Pro	Thr	Thr	Thr 2980		Ile	Thr	Thr	Thr 2985		Thr	Val	Thr	Pro 2990		Pro
Thr	Pro	Thr 2995	_	Thr	Gln	Thr	Pro 3000		Thr	Thr	Pro	Ile 3005		Thr	Thr
Thr	Thr 3010		Thr	Pro	Thr	Pro 3015		Pro	Thr	Gly	Thr 3020		Thr	Pro	Thr
Thr 3025		Pro	Ile	Thr	Thr 3030	Thr	Thr	Thr	Val	Thr 3035		Thr	Pro	Thr	Pro 3040
Thr	Gly	Thr	Gln	Thr 3045		Thr	Thr	Thr	Pro 3050		Thr	Thr	Thr	Thr 3055	

- Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr 3060 3065 3070
- Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly 3075 3080 3085
- Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr 3090 3095 3100
- Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile 3105 3110 3115 3120
- Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln 3125 3130 3135
- Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr 3140 3145 3150
- Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr 3155 3160 3165
- Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro 3170 3175 3180
- Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr 3185 3190 3195 3200
- Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr 3205 3210 3215
- Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr 3220 3225 3230
- Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr 3235 3240 3245
- Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val 3250 3255 3260
- Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro 3265 3270 3275 3280
- Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr 3285 3290 3295
- Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro 3300 3310
- Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr 3315 3320 3325
- Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr 3330 3335 3340
- Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro 3345 3350 3355 3360

PCT/US00/35596 WO 01/49716

Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr

Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr

Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro

Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr

Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr

Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly

Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr

Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile

Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln

Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr

Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr

Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro

Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr

Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr

Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr

Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr

Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val

Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro

Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr

Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro

366	5				367	0				367	5				3680
Thr	Pro	Thr	Pro	Thr 368	Gly 5	Thr	Gln	Thr	Pro 369		Thr	Thr	Pro	Ile 369	
Thr	Thr	Thr	Thr 370	Val)	Thr	Pro	Thr	Pro 370		Pro	Thr	Gly	Thr 3710		Thr
Pro	Thr	Thr 371	Thr 5	Pro	Ile	Thr	Thr 372		Thr	Thr	Val	Thr 372		Thr	Pro
Thr	Pro 373	Thr 0	Gly	Thr	Gln	Thr 373		Thr	Thr	Thr	Pro 374		Thr	Thr	Thr
Thr 374	Thr 5	Val	Thr	Pro	Thr 375	Pro O	Thr	Pro	Thr	Gly 375		Gln	Thr	Pro	Thr 3760
Thr	Thr	Pro	Ile	Thr 376		Thr	Thr	Thr	Val 3770		Pro	Thr	Pro	Thr 3775	
Thr	Gly	Thr	Gln 3780	Thr	Pro	Thr	Thr	Thr 3785		Ile	Thr	Thr	Thr 3790		Thr
Val	Thr	Pro 379	Thr	Pro	Thr	Pro	Thr 3800		Thr	Gln	Thr	Pro 3805		Thr	Thr
Pro	Ile 3810	Thr)	Thr	Thr	Thr	Thr 3815		Thr	Pro	Thr	Pro 3820		Pro	Thr	Gly
Thr 382	Gln 5	Thr	Pro	Thr	Thr 3830		Pro	Ile	Thr	Thr 3835		Thr	Thr	Val	Thr 3840
Pro	Thr	Pro	Thr	Pro 3845		Gly	Thr	Gln	Thr 3850		Thr	Thr	Thr	Pro 3855	
Thr	Thr	Thr	Thr 3860		Val	Thr	Pro	Thr 3865		Thr	Pro	Thr	Gly 3870		Gln
Thr	Pro	Thr 3875		Thr	Pro	Ile	Thr 3880		Thr	Thr	Thr	Val 3885		Pro	Thr
Pro	Thr 3890	Pro	Thr	Gly	Thr	Gln 3895		Pro	Thr	Thr	Thr 3900		Ile	Thr	Thr
Thr 3905	Thr	Thr	Val	Thr	Pro 3910		Pro	Thr		Thr 3915		Thr	Gln	Thr	Pro 3920
Thr	Thr	Thr		Ile 3925		Thr	Thr	Thr	Thr 3930		Thr	Pro	Thr	Pro 3935	
Pro	Thr	Gly	Thr 3940	Gln	Thr	Pro	Thr	Thr 3945		Pro	Ile	Thr	Thr 3950		Thr
Thr	Val	Thr 3955	Pro	Thr	Pro		Pro 3960		Gly	Thr	Gln	Thr 3965		Thr	Thr
Thr	Pro 3970	Ile	Thr	Thr		Thr 3975		Val	Thr		Thr 3980		Thr	Pro	Thr

PCT/US00/35596 WO 01/49716

Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Thr Pro Ile Thr Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Pro Thr Thr Pro Ile Thr Thr Thr Thr Val Thr Pro Thr Pro Thr Pro Thr Gly Thr Gln Thr Gly Pro Pro Thr His Thr Ser Thr Ala Pro Ile Ala Glu Leu Thr Thr Ser Asn Pro Pro Pro Glu Ser Ser Thr Pro Gln Thr Ser Arg Ser Thr Ser Ser Pro Leu Thr Glu Ser Thr Thr Leu Leu Ser Thr Leu Pro Pro Ala Ile Glu Met Thr Ser Thr Ala Pro Pro Ser Thr Pro Thr Ala Pro Thr Thr Thr Ser Gly Gly His Thr Leu Ser Pro Pro

Ser Thr Thr Thr Ser Pro Pro Gly Thr Pro Thr Arg Gly Thr Thr Thr

- Gly Ser Ser Ser Ala Pro Thr Pro Ser Thr Val Gln Thr Thr Thr 4290 4295 4300
- Ser Ala Trp Thr Pro Thr Pro Thr Pro Leu Ser Thr Pro Ser Ile Ile 4305 4310 4315 4320
- Arg Thr Thr Gly Leu Arg Pro Tyr Pro Ser Ser Val Leu Ile Cys Cys 4325 4330 4335
- Val Leu Asn Asp Thr Tyr Tyr Ala Pro Gly Glu Glu Val Tyr Asn Gly 4340 4345 4350
- Thr Tyr Gly Asp Thr Cys Tyr Phe Val Asn Cys Ser Leu Ser Cys Thr 4355 4360 4365
- Leu Glu Phe Tyr Asn Trp Ser Cys Pro Ser Thr Pro Ser Pro Thr Pro 4370 4375 4380
- Thr Pro Ser Lys Ser Thr Pro Thr Pro Ser Lys Pro Ser Ser Thr Pro 4385 4390 4395 4400
- Ser Lys Pro Thr Pro Gly Thr Lys Pro Pro Glu Cys Pro Asp Phe Asp 4405 4410 4415
- Pro Pro Arg Gln Glu Asn Glu Thr Trp Trp Leu Cys Asp Cys Phe Met 4420 4425 4430
- Ala Thr Cys Lys Tyr Asn Asn Thr Val Glu Ile Val Lys Val Glu Cys 4435 4440 4445
- Glu Pro Pro Pro Met Pro Thr Cys Ser Asn Gly Leu Gln Pro Val Arg
 4450 4455 4460
- Val Glu Asp Pro Asp Gly Cys Cys Trp His Trp Glu Cys Asp Cys Tyr 4465 4470 4475 4480
- Cys Thr Gly Trp Gly Asp Pro His Tyr Val Thr Phe Asp Gly Leu Tyr 4485 4490 4495
- Tyr Ser Tyr Gln Gly Asn Cys Thr Tyr Val Leu Val Glu Glu Ile Ser 4500 4505 4510
- Pro Ser Val Asp Asn Phe Gly Val Tyr Ile Asp Asn Tyr His Cys Asp 4515 4520 4525
- Pro Asn Asp Lys Val Ser Cys Pro Arg Thr Leu Ile Val Arg His Glu 4530 4535 4540
- Thr Gln Glu Val Leu Ile Lys Thr Val His Met Met Pro Met Gln Val 4545 4550 4555 4560
- Gln Val Gln Val Asn Arg Gln Ala Val Ala Leu Pro Tyr Lys Lys Tyr 4565 4570 4575
- Gly Leu Glu Val Tyr Gln Ser Gly Ile Asn Tyr Val Val Asp Ile Pro 4580 4585 4590
- Glu Leu Gly Val Leu Val Ser Tyr Asn Gly Leu Ser Phe Ser Val Arg .

		4595	5				4600)				4605	5		
Leu	Pro 4610	_	His	Arg	Phe	Gly 4615		Asn	Thr	Lys	Gly 4620		Cys	Gly	Thr
Cys 4625		Asn	Thr	Thr	Ser 4630	-	Asp	Cys	Ile	Leu 4635		Ser	Gly	Glu	Ile 4640
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Ser	Cys	Phe	Met	Pro 4725	_	Ser	Ser	Leu	Glu 4730		Ala	Ser		Gln 4735	
Tyr	Ala	Ala	Leu 4740	_	Ala	Gln	Gln	Asn 4745		Cys	Leu	Asp	Trp 4750	Arg)	Asn
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Asn	Ile	Thr	Val	Cys 4885	_	Суз	Asn	Thr	Ser 4890		Cys	Lys	Glu	Lys 4895	
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- Gly Asn Ala Glu Tyr Gln Pro Gly Ser Pro Val Tyr Ser Ser Lys Cys 4930 4940
- Gln Asp Cys Val Cys Thr Asp Lys Val Asp Asn Asn Thr Leu Leu Asn 4945 4950 4955 4960
- Val Ile Ala Cys Thr His Val Pro Cys Asn Thr Ser Cys Ser Pro Gly
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- Phe Glu Leu Met Glu Ala Pro Gly Glu Cys Cys Lys Lys Cys Glu Gln 4980 4985 4990
- Thr His Cys Ile Ile Lys Arg Pro Asp Asn Gln His Val Ile Leu Lys 4995 5000 5005
- Pro Gly Asp Phe Lys Ser Asp Pro Lys Asn Asn Cys Thr Phe Phe Ser 5010 5015 5020
- Cys Val Lys Ile His Asn Gln Leu Ile Ser Ser Val Ser Asn Ile Thr 5025 5030 5035 5040
- Cys Pro Asn Phe Asp Ala Ser Ile Cys Ile Pro Gly Ser Ile Thr Phe 5045 5050 5055
- Met Pro Asn Gly Cys Cys Lys Thr Cys Thr Pro Arg Asn Glu Thr Arg 5060 5065 5070
- Val Pro Cys Ser Thr Val Pro Val Thr Thr Glu Val Ser Tyr Ala Gly 5075 5080 5085
- Cys Thr Lys Thr Val Leu Met Asn His Cys Ser Gly Ser Cys Gly Thr 5090 5095 5100
- Phe Val Met Tyr Ser Ala Lys Ala Gln Ala Leu Asp His Ser Cys Ser 5105 5110 5115 5120
- Cys Cys Lys Glu Glu Lys Thr Ser Gln Arg Glu Val Val Leu Ser Cys 5125 5130 5135
- Pro Asn Gly Gly Ser Leu Thr His Thr Tyr Thr His Ile Glu Ser Cys 5140 5150
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Arg Asn Trp Ser Asp Ala Glu Leu Glu Cys Gln Ser Tyr Gly Asn Gly 50

Ala His Leu Ala Ser Ile Leu Ser Leu Lys Glu Ala Ser Thr Ile Ala 70

Glu Tyr Ile Ser Gly Tyr Gln Arg Ser Gln Pro Ile Trp Ile Gly Leu 90

His Asp Pro Gln Lys Arg Gln Gln Trp Gln Trp Ile Asp Gly Ala Met 100

Tyr Leu Tyr Arg Ser Trp Ser Gly Lys Ser Met Gly Gly Asn Lys His 120

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Arg Asn Trp Ser Asp Ala Glu Leu Glu Cys Gln Ser Tyr Gly Asn Gly 50 55

339

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His Asp Pro Gln Lys Arg Gln Gln Trp Gln Trp Ile Asp Gly Ala Met
100 105 110

Tyr Leu Tyr Arg Ser Trp Ser Gly Lys Ser Met Gly Gly Asn Lys His 115 120 125

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PCT/US00/35596 WO 01/49716

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Ala His Leu Ala Ser Ile Leu Ser Leu Lys Glu Ala Ser Thr Ile Ala 65 70

Glu Tyr Ile Ser Gly Tyr Gln Arg Ser Gln Pro Ile Trp Ile Gly Leu

His Asp Pro Gln Lys Arg Gln Gln Trp Gln Trp Ile Asp Gly Ala Met

Tyr Leu Tyr Arg Ser Trp Ser Gly Lys Ser Met Gly Gly Asn Lys His 115

Cys Ala Glu Met Ser Ser Asn Asn Phe Leu Thr Trp Ser Ser Asn 135

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Pro Met Thr Phe Ser Ile Tyr Glu Gly Gln Glu Pro Ser Gln Ile Ile

Phe Gln Phe Lys Ala Asn Pro Pro Ala Val Thr Phe Glu Leu Thr Gly

Glu Thr Asp Asn Ile Phe Val Ile Glu Arg Glu Gly Leu Leu Tyr Tyr 65 75 70

Asn Arg Ala Leu Asp Arg Glu Thr Arg Ser Thr His Asn Leu Gln Val

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				85					90					95	
Ala	Ala	Leu	Asp 100	Ala	Asn _.	Gly	Ile	Ile 105	Val	Glu	Gly	Pro	Val 110	Pro	Ile
Thr	Ile	Glu 115	Val	Lys	Asp	Ile	Asn 120	Asp	Asn	Arg	Pro	Thr 125	Phe	Leu	Gln
Ser	Lys 130	Tyr	Glu	Gly	Ser	Val 135	Arg	Gln	Asn	Ser	Arg 140	Pro	Gly	Lys	Pro
Phe 145	Leu	Tyr	Val	Asn	Ala 150	Thr	Asp	Leu	Asp	Asp 155	Pro	Ala	Thr	Pro	Asn 160
Gly	Gln	Leu	Tyr	Tyr 165	Gln	Ile	Val	Ile	Gln 170	Leu	Pro	Met	Ile	Asn 175	Asn
Val	Met	Tyr	Phe 180	Gln	Ile	Asn	Asn	Lys 185	Thr	Gly	Ala	Ile	Ser 190	Leu	Thr
Arg	Glu	Gly 195	Ser	Gln	Glu	Leu	Asn 200	Pro	Ala	Lys	Asn	Pro 205	Ser	Tyr	Asn
Leu	Val 210	Ile	Ser	Val	Lys	Asp 215	Met	Gly	Gly	Gln	Ser 220	Glu	Asn	Ser	Phe
Ser 225	Asp	Thr	Thr	Ser	Val 230	Asp	Ile	Ile	Val	Thr 235	Glu	Asn	Ile	Trp	Lys 240
Ala	Pro	Lys	Pro	Val 245	Glu	Met	Val	Glu \	Asn 250	Ser	Thr	Asp	Pro	His 255	Pro
Ile	Lys	Ile	Thr 260	Gln	Val	Arg	Trp	Asn 265	Asp	Pro	Gly	Ala	Gln 270	Tyr	Ser
Leu	Val	Asp 275	Lys	Glu	Lys	Leu	Pro 280	Arg	Phe	Pro	Phe	Ser 285	Ile	Asp	Gln
Glu	Gly 290	Asp	Ile	Tyr	Val.	Thr 295	Gln	Pro	Leu	Asp	Arg 300	Glu	Glu	Lys	Asp
Ala 305	Tyr	Val	Phe	Tyr	Ala 310	Val	Ala	ГÀЗ	Asp	Glu 315	Tyr	Gly	Lys	Pro	Leu 320
Ser	Tyr	Pro	Leu	Glu 325	Ile	His	Val	ГÀЗ	Val 330	Lys	Asp	Ile	Asn	Asp 335	Asn
Pro	Pro	Thr	Cys 340	Pro	Ser	Pro	Val	Thr 345	Val	Phe	Glu	Val	G1n 350	Glu	Asn
Glu	Arg	Leu 355	Gly	Asn	Ser	Ile	Gly 360	Thr	Leu	Thr	Ala	His 365	Asp	Arg	Asp
Glu	Glu 370	Asn	Thr	Ala	Asn	Ser 375	Phe	Leu	Asn	Tyr	Arg 380	Ile	Val	Glu	Gln
Thr 385	Pro	Lys	Leu	Pro	Met 390	Asp	Gly	Leu	Phe	Leu 395	Ile	G1n	Thr	Tyr	Ala 400

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Gly	Met	Leu	Gln	Leu 405	Ala	Lys	Gln	Ser	Leu 410	Lys	Lys	Gln	Asp	Thr 415	Pro
Gln	Tyr	Asn	Leu 420	Thr	Ile	Glu	Val	Ser 425	Asp	Lys	Asp	Phe	Lys 430	Thr	Leu
Cys	Phe	Val 435	Gln	Ile	Asn	Val	Ile 440	Asp	Ile	Asn	Asp	Gln 445	Ile	Pro	Ile
Phe	Glu 450	Lys	Ser	Asp	Tyr	Gly 455	Asn	Leu	Thr	Leu	Ala 460	Glu	Asp	Thr	Asn
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Phe	Thr	Gly	Ser	Ser 485	Lys	Ile	Leu	Tyr	His 490	Ile	Ile	Lys	Gly	Asp 495	Ser
Glu	Gly	Arg	Leu 500	Gly	Val	Asp	Thr	Asp 505	Pro	His	Thr	Asn	Thr 510	Gly	Tyr
Val	Ile	Ile 515	Lys	Lys	Pro	Leu	Asp 520	Phe	Glu	Thr	Ala	Ala 525	Val	Ser	Asn
Ile	Val 530	Phe	Lys	Ala	Glu	Asn 535	Pro	Glu	Pro	Leu	Val 540	Phe	Gly	Val	Lys
Tyr 545	Asn	Ala	Ser	Ser	Phe 550	Ala	Lys	Phe	Thr	Leu 555	Ile	Val	Thr	Asp	Val 560
Asn	Glu	Ala	Pro	Gln 565	Phe	Ser	Gln	His	Val 570	Phe	Gln	Ala	Lys	Val 575	Ser
Glu	Asp	Val	Ala 580	Ile	Gly	Thr	Lys	Val 585	Gly	Asn	Val	Thr	Ala 590	Lys	Asp
Pro	Glu	Gly 595	Leu	Asp	Ile	Ser	Tyr 600	Ser	Leu	Arg	Gly	Asp 605	Thr	Arg	Gly
Trp	Leu 610	Lys	Ile	Asp	His	Val 615	Thr	Gly	Glu	Ile	Phe 620	Ser	Val	Ala	Pro
Leu 625	Asp	Arg	Glu	Ala	Gly 630	Ser	Pro	Tyr	Arg	Val 635	Gln	Val	Val	Ala	Thr 640
Glu	Val	Gly	Gly	Ser 645	Ser	Leu	Ser	Ser	Val 650	Ser	Glu	Phe	His	Leu 655	Ile
Leu	Met	Asp	Val 660	Asn	Asp	Asņ	Pro	Pro 665	Arg	Leu	Ala	Lys	Asp 670	Tyr	Thr
Gly	Leu	Phe 675	Pḥe	Cys	His	Pro	Leu 680	Ser	Ala	Pro	Gly	Ser 685	Leu	Ile	Phe
Glu	Ala 690	Thr	Asp	Asp	Asp	Gln 695	His	Leu	Phe	Arg	Gly 700	Pro	His	Phe	Thr

705	ser	ьeu	GТĀ	Ser	710	Ser	ьeu	GIN	Asn	715	Trp	GIU	vaı	ser	Lys 720	
Ile	Asn	Gly	Thr	His 725	Ala	Arg	Leu	Ser	Thr 730	Arg	His	Thr	Asp	Phe 735	Glu	
Glu	Arg	Ala	Tyr 740	Val	Val	Leu	Ile	Arg 745	Ile	Asn	Asp	Gly	Gly 750	Arg	Pro	
Pro	Leu	Glu 755	Gly	Ile	Val	Ser	Leu 760	Pro	Val	Thr	Phe	Cys 765	Ser	Cys	Val	
Glu	Gly 770	Ser	Cys	Phe	Arg	Pro 775	Ala	Gly	His	Gln	Thr 780	Gly	Ile	Pro	Thr	
Val 785	Gly	Met	Ala	Val	Gly 790	Ile	Leu	Leu	Thr	Thr 795	Leu	Leu	Val	Ile	Gly 800	
Ile	Ile	Leu	Ala	Val 805	Val	Phe	Ile	Arg	Ile 810	Lys	Lys	Asp	Lys	Gly 815	Lys	
Asp	Asn	Val	Glu 820	Ser	Ala	Gln	Ala	Ser 825	Glu	Val	Lys	Pro	Leu 830	Arg	Ser	
<213 <213 <213	0> 10 L> 26 2> DN 3> Ho	SS NA . omo s	sapie	ens												
gaaa tgct tcaq aaca	acato gcct gattt	gga d ga t ga g at t	caaag gcatt caagt	gtgad aaca gggg	ca ct ag gt ga ct	tagat tattt taaaa	tgtad tcad	c cad	gctga actto	agtg gact	ttta tcaa	aatct atato	ctc o	cato	ataata cacaga gtgagg atcttc	120 180
<213 <212)> 10 l> 44 2> PF 3> Ho	! (T	sapie	ens												
)> 10 Met		Cys	Pro 5	Leu	Asn ·	Phe	Asp	Cys 10	Pro	Lys	Asn	Leu	Phe 15	Leu	
Ile	Tyr	Asn	Met 20	Leu	Pro	Asp	Lys	Val 25	Thr	Leu	Asp	Val	Pro 30	Ala	Glu	
Суз	Leu	Ile 35	Phe	Pro	Ser	Gln	Ile 40	Arg	Phe	Glu	His					

(19) World Intellectual Property Organization International Bureau





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09/575,251	19 May 2000 (19.05.2000)	US
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- (74) Agents: POTTER, Jane, E., R.: Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 et al. (US).
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Published:

- with international search report
- (88) Date of publication of the international search report: 31 January 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

A3

(54) Title: COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as colon cancer, are disclosed. Compositions may comprise one or more colon tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a colon tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as colon cancer. Diagnostic methods based on detecting a colon tumor protein, or mRNA encoding such a protein, in a sample are also provided.



INTERNATIONAL SEARCH KEPUKI

In. ational Application No PCT/US 00/35596

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N15/62 C07K14/47 C07K16/14 C

G01N33/53 G01N33/574 A61K39/00

C07K16/14 C12Q1/68 A61K39/395 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C07K C12Q G01N A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, SEQUENCE SEARCH

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	US 5 929 033 A (TANG, Y.T. ET AL.) 27 July 1999 (1999-07-27)	1,2,4,5, 7-17,21, 31,40-60
A	abstract; figure 1 column 2, line 46 -column 4, line 14 column 4, line 62 -column 19, line 38 column 20, line 42 -column 27, line 30 column 27, line 63 -column 29, line 29 column 32 -column 37; examples 4-12 SEQ ID NOS: 1 and 2 column 37 -column 44 column 45 -column 46; claims 1-14,17,18	6,18-39

X Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.
 Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
9 August 2001	3 0. 10. 01
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2	Authorized officer
NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fuchs, U

2

INTERNATIONAL SEARCH REPORT

Inte ional Application No PCT/US 00/35596

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category "	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 99 60161 A (DIADEXUS LLC) 25 November 1999 (1999-11-25) abstract page 2, line 34 -page 11, line 30 clone ID NO: 2348122, SEQ ID NOS: 7 and 10 page 13, line 1 -page 16, line 6; table 1 page 28, line 1 -page 31, line 25; table 9 page 32 -page 33; claims 1-6	1,2,4,5, 7-16, 40-60 6,17-39
X	WO 99 63088 A (GENENTECH, INC.) 9 December 1999 (1999-12-09)	1,2,4,5, 7-17,58, 59
A	abstract page 1, line 23 -page 2, line 6 PR0698 page 7, line 19 - line 29 page 63, line 33 -page 64, line 15 page 280, line 25 -page 284, line 23 page 286, line 16 - line 19 page 300, line 36 - line 37 page 317, line 24 - line 30 page 364, line 10 - line 32 page 365, line 16 -page 373, line 20 page 391 -page 392; example 19 page 488 -page 495; examples 139-145 ATCC DEP NO: 209904 page 497; table 2 page 501 -page 508; claims 1-26 page 546 -page 548; figures 37-39	40-57,60
х	WO 99 01020 A (HUMAN GENOME SCIENCES, INC.) 14 January 1999 (1999-01-14)	1,4, 7-22,31, 54-60
A	abstract	2,5,6, 23-30, 32-53
	page 2, line 1 - line 8 gene ID NO: 13 page 22, line 15 -page 24, line 10 page 34 -page 54, line 37; table 1 page 57, line 7 - line 32 page 63, line 1 -page 70, line 5 SEQ ID NO: 23 page 129 -page 130 SEQ ID NO: 85 page 162 -page 163 page 174 -page 177; claims 1-17,19,21	

INTERNATIONAL SEARCH REPORT

Int ational Application No PCT/US 00/35596

		PCT/US 00/35596
C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category "	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL, HEIDELBERG, FRG [Online] 12 November 1998 (1998-11-12) LIU, W.L. ET AL.: "Homo sapiens GW112 protein (GW112) mRNA, complete cds" Database accession no. AF097021 XP002174317	1,4, 7-10,12, 16,58,59
X	the whole document -& DATABASE EMBL, HEIDELBERG, FRG [Online] GW112 protein, 1 May 1999 (1999-05-01) LIU, W.L. ET AL.: "Identification and characterization of novel full-length cDNAs differentially expressed in human hematopoietic lineages" retrieved from HOMO SAPIENS Database accession no. 095362 XP002174318 the whole document	1,4, 7-10,12, 16,58,59
X	DATABASE EMBL, HEIDELBERG, FRG [Online] 18 April 1997 (1997-04-18) ADAMS, M.D. ET AL.: "EST77899 Pancreas tumor III Homo sapiens cDNA 5' end similar to olfactomedin" Database accession no. AA366895 XP002174319 the whole document	1,4, 7-10,12, 16,58,59
P,X	WO 00 37643 A (CORIXA CORPORATION) 29 June 2000 (2000-06-29) contig ID NO: 2 the whole document	1,2,4-60
P,X	WO 00 73348 A (GENENTECH, INC.) 7 December 2000 (2000-12-07) abstract page 1, line 1 -page 6, line 37 PR0698 page 7, line 18 - line 21 page 47, line 1 -page 70, line 27 page 79 -page 81; example 8 page 95 -page 106; examples 26-33 page 107 -page 122; example 36; table 7 page 124 -page 130; claims 1-40 page 139 -page 140; figures 9,10 -/	1,2,4,5, 7-17,21, 31,40-60

INTERNATIONAL SEARCH REPORT

Intervional Application No PCT/US 00/35596

		PC1/US 00/35596
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category 3	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 21991 A (GENETICS INSTITUTE, INC.) 20 April 2000 (2000-04-20) abstract SEQ ID NO: 463 clone ID NO: IJ1193 page 3, line 1 -page 104, line 17; table 2 page 121, line 1 -page 127, line 11 page 130; table 3 page 135 -page 200; claims 1-8	1,2,4,5, 7-17,58, 59
Р,Х	figure P123 WO 00 55350 A (HUMAN GENOME SCIENCES, INC.) 21 September 2000 (2000-09-21)	1,4, 7-22,31, 54-60
	abstract page 2, line 17 -page 11, line 7 SEQ ID NO: 445 page 70; table 1 page 119, line 1 -page 124, line 2 contig ID NO: 840608 page 208; table 3 page 241, line 1 -page 255, line 32 page 284, line 1 -page 372, line 4 page 375, line 6 -page 381, line 11 page 415, line 24 -page 421, line 22 page 423, line 29 -page 432, line 13 page 602; claims 1-17,19,21 SEQ ID NO: 445 figures P375-P377 SEQ ID NO: 1287 figures P1319-P1322	
Ε	WO 01 42285 A (INCYTE GENOMICS, INC.) 14 June 2001 (2001-06-14) abstract page 4, line 33 -page 9, line 32 page 23, line 29 -page 33, line 31 page 35, line 32 -page 55, line 8 SEQ ID NO: 17 page 78; table 2 SEQ ID NO: 38 page 83; table 3 page 89 -page 91; claims 1-17,23,24 page 108 -page 110 page 129 -page 130	1,2,4,5, 7-17,21, 31,40-60
- Children	-/	

INTERNATIONAL SEARCH REPURI

Int tional Application No
PCT/US 00/35596

		PC1/03 00/33390
C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	US 6 183 968 B1 (BANDMAN, O. ET AL.) 6 February 2001 (2001-02-06) abstract	1,2,4,5, 7-10, 12-16, 48,50, 51,53, 58-60
	column 1, line 54 -column 2, line 35 column 3, line 61 -column 12, line 58 SEQ ID NO: 127 column 21 -column 22; table 1 column 191 -column 194 column 205 -column 206; claims 1,3,5-7	
A	WO 98 53319 A (JOHNS HOPKINS UNIVERSITY) 26 November 1998 (1998-11-26) the whole document	1,2,4-60
A	SJÖGREN, H.O.: "Therapeutic immunization against cancer antigens using genetically engineered cells" IMMUNOTECHNOLOGY, vol. 3, no. 3, October 1997 (1997-10), pages 161-172, XP004097000 the whole document	23-31, 35-39
A	EP 0 317 141 A (BECTON DICKINSON AND COMPANY) 24 May 1989 (1989-05-24) the whole document	32-34

PCT/US 00/35596

INTERNATIONAL SEARCH REPORT

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)	
This Int	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	_
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:	
	Although claims 21, 22, 29-31, 34, 37-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.	
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:	
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)	
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:	
	see additional sheet	
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.	
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.	
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:	
4. X	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1,2,4-60 partially	
Remark	on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 2, 4-60 partially

Invention 1

An isolated polypeptide comprising at least an immunogenic portion of a colon tumor protein wherein the tumor protein comprises an amino acid sequence being encoded by the polynucleotide sequence SEQ ID NO: 2, variants of said polypeptide, fusion proteins comprising said polypeptide, polynucleotides or oligonucleotides derived from said polynucleotide, antibodies or fragments thereof binding to said polypeptide, diagnostic kits comprising said oligonucleotides or antibodies, pharmaceutical compositions and vaccines comprising said products or comprising antigen-presenting cells expressing said polypeptide and their use in methods for inhibiting, monitoring or diagnosing the development of a colon cancer, for removing tumor cells from a a sample or for expanding and / or stimulating T-cells;

2. Claims: 1, 2, 4-60 partially

Invention 2

idem as subject 1 but limited to SEQ ID NO: 8;

3. - 73. Claims: 1, 2, 4-60 partially

Inventions 3-73

idem as subject 1 but limited to SEQ ID NOS: 15-184 as described in claim 1;

74. Claims: 1-60 partially

Invention 74

idem as subject 1 but limited to SEQ ID NO: 189 and an isolated polypetide comprising SEQ ID NO: 200;

75. - 659. Claims: 1, 2, 4-60 partially

Inventions 75-659

idem as subject 1 but limited to SEQ ID NOS: 191-1081 as described in claim 1;

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

660. - 666. Claims: 3 partially

Inventions 660-666

isolated polypetides comprising SEQ ID NOS: 198-204;

667. - 1072. Claims: 25-53 partially

Inventions 667-1072

a vaccine comprising antigen-presenting cells expressing a polypeptide comprising at least an immunogenic portion of a colon tumor protein wherein the tumor protein comprises an amino acid sequence being encoded by the polynucleotide sequences SEQ ID NOS: 1-121, 123-197, 205-630, 632-684, 686, 690, 691, 694-1081 (in so far as not being mentioned in claim 1) and the use of said polypeptides, polynucleotides and antigen-presenting cells in methods for inhibiting, monitoring or diagnosing the development of a colon cancer, for removing tumor cells from a a sample or for expanding and / or stimulating T-cells.

page 2 of 2

IN LEKNA LIUNAL SEARCH REFURI

Information on patent family members

Int tional Application No PCT/US 00/35596

					<u> </u>		00/35596
	atent document d in search report		Publication date		Patent family member(s)		Publication date
US	5929033	Α	27-07-1999	NONE			
WO	9960161	А	25-11-1999	EP WO	1080227 9960161		07-03-2001 25-11-1999
WO	9963088	Α	09-12-1999	AU WO AU WO	4328699 9963088 2212299 9935176	8 A2 9 A	20-12-1999 09-12-1999 26-07-1999 15-07-1999
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